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A REPORT ON THE MANAGEMENT OF BURNS

USING THE OCCLUSIVE COMPRESSION DRESSING, WITH SULFATHIAZOLE EMULSION

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IN THE NOVEMBER, 1942, number of the ANNALS OF SURGERY, the authors[1] reviewed the problem of the treatment of burns and set forth their conception of the principles upon which this should be based, the essence of the matter being that a burn is a large wound and should be treated as such. They, furthermore, suggested that fundamentally all treatment should be timed to anticipate the dangers and difficulties arising from severe burns, namely shock, toxemia and infection, with their sequelae of death or disability. From this broad conception of the problem they evolved a system or method of treatment divided into general and local measures. This plan was based upon a practical timing chart which was intended to be a ready reference to all doctors and nurses handling burns. In selecting the measures for treatment they attempted to embrace the best methods of dealing with the problem having due regard for (a) fundamental surgical practice in the treatment of all wounds; and (b) the experience of others with practical knowledge of the problem. The details of the plan and principles are reviewed briefly in the following schema:

TIMING IN THE TREATMENT OF BURNS (see operational chart)

General Measures: To anticipate and prevent shock, toxemia and infection —with death, sepsis and inanition:

1. Retention of body heat by a burn tent or other measure.
2. Prevention of pain by adequate sedation.
3. Control of hemoconcentration and other blood changes by the regulated use of blood, plasma, serum, *etc.*
4. Controlled administration of fluids and the necessary amount of carbohydrate and protein food either by infusion or by mouth.
5. Specific antisera such as antitetanic and antigas.
6. Gentle handling to avoid pain and fatigue.
7. Delay in carrying out any local treatment until antishock measures are at least well advanced, and control in view. This rule is operative in the

treatment of all wounds. If necessary, local treatment already commenced should be interrupted if signs of shock recur.

8. Avoidance of anesthetics whenever possible to prevent further shock and depression of general condition.

9. Promotion of renal output by adequate fluids administered by vein or mouth.

Local Measures: To anticipate and prevent infection and maiming, with disability or death, and, conversely, to promote rapid healing:

1. Gentle surgical wound cleansing with soap and water, saline and, when necessary, some other detergent.

2. Removal of débris, and surgical excision of dead and devitalized tissues. This includes the opening of blebs.

3. Employment of occlusive bulky pressure dressings, infrequently changed, to promote:

(a) Rest by immobilization, resulting in lymphstasis.
(b) Prevention of bacterial contamination by exclusion.
(c) Pressure (1) to prevent edema and thereby improve the circulation of the blood; (2) to minimize the lymphatic flow.
(d) Drainage into the bulky absorptive dressing of discharge from the burned surface.
(e) Bacteriostatis: 1. Autogenous. 2. Bacteriostatic sulfonamides,* *etc.*

4. Employment of the earliest possible skin grafting.
(a) Primary, when possible, though rarely practicable.
(b) Delayed primary as the common practice.
(c) Secondary when made necessary by very deep and extensive burns or by delay for some special reason.
(d) Homografts when necessary to save life or minimize inanition.

The authors have completed a review of two years experience with well over 200 major and minor burns treated according to the plan outlined. From this group of cases, 100 major burns, requiring hospitalization, have been selected for particular analysis. The remainder, mainly treated in the out-patient department, require only the statement that they have shown equally satisfactory results under less adequate control. Incidentally, a considerable number of frost-bites were treated with similar success by this method. For detailed study of the major burns treated in hospital and to make the analysis more comprehensive, they have been broken down for study into three groups as follows:

Group (A)—According to area of body surface involved.
Group (B)—According to the depth of the burn.
Group (C)—According to the results of treatment.

For simplicity's sake Groups A and B will be dealt with rather briefly, leaving C for more detailed analysis.

* A five per cent oil-in-water emulsion of sulfathiazole (M. G. H. formula[1]) has been used almost exclusively for this series.

TIMING IN THE INFREQUENT OCCLUSIVE PR

PERIOD OF SHOCK 48 HOURS

	First Hour	First 24 Hours	Second 24 Hours
General Treatment	Hypo Morphine ¼ gr. (Intravenous) if necessary Repeat in the hour if necessary	Repeat Morphine as may be indicated during this period	
Shock Team 24 hour service **Under Supervision of Senior Surgeon**		Cortin 50 cc. (optional) in extreme cases	Repeat Cortin Intramuscularly 20 cc. 30 cc. Q. 6 H. as indicated for 48 hours
	Intravenous Therapy Plasma or Serum In amounts of 500 cc. First 500 cc. given rapidly	Continue to a minimum of 1,000 cc. (Plasma or Serum) for 10% burn i by continuous intravenous drip. Control the amount of serum or plasma globin, Hematocrit and Plasma Proteins—as well as clinical observation	
	10% Glucose only if indicated	Intravenous 10% Glucose as indicated, add saline if vomiting	
	External Heat—Develop slowly to 70°F. under tent	**SERA** A.-T.-S.—3000 units Anti-Gas Serum when indicated	
	Water by mouth containing carbohydrate for first 24 hours		Fluids—As tolerated high in Carbohydrate
	Oxygen by B.L.B. apparatus or tent—when indicated		Continue Oxygen as indicated
			Enema
Local Treatment **Burn Team** **Under Supervision of Senior Surgeon**	Delayed until Intravenous Shock Treatment begun and effective	**Operation** Without anesthetic using pure soap lather (detergent when necessary)	
		Mechanical removal of débris, dirt and dead tissue	
		Open blebs	No dressing change
		All Burns **Occlusive pressure dressing** over 5% Sulfathiazole Emulsion (Ann. Surg. Nov. 1942—Vol. 116, — page 641)	
Laboratory Examinations	Hemoglobin Estimation or Hematocrit and Plasma Proteins	Repeat Q. 1 h. until Hemo-concentration controlled and thereafter at least Q. 4 h.	Continue Hematocrit, Hgb. and Plasma Proteins Q. 4 H.
			Blood Chemistry Plasma Proteins Chlorides Sugar Sulfonamide Level
	R.B.C. Count	**Culture** of burned surface before treatment	
	Uranalysis	Uranalysis	Uranalysis
Clinical Data		Chart P. & B.P. Q. 1 hr. Hematocrit Plasma Proteins } Q. 4 H. Hemoglobin % Temperature	T.-P.-R. Q. 4 H. B.P. and P. Chart Q. 1 H. Hematocrit, Hemoglobin and Plasma Proteins
	Admission T.-P.-R. and Blood Pressure		
Chart		Intake and output daily Plasma. Serum. Glucose. Saline. Blood Chemistry Sera	Intake and output daily amou types of infusions separately units

HE INFREQUENT OCCLUSIVE PRESSURE DRESSING TREATMENT OF M

ERIOD OF SHOCK 48 HOURS urs Second 24 Hours	TOXEMIA PERIOD 2nd to 5th Day
be indicated during this period	Morphine or Barbiturates as indicated
Repeat Cortin Intramuscularly 20 cc. 30 cc. Q. 6 H. as indicated for 48 hours	**Sulfonamides orally or intravenously** is below 1000 cc. per day
of 1,000 cc. (Plasma or Serum) for 10% burn in urs s drip. Control the amount of serum or plasma b mo- lasma Proteins—as well as clinical observation	**Blood Substitutes** as indicated
as indicated, add saline if vomiting	Glucose as indicated, by blood chemistry **Saline** only when blood chlorides depleted
icated	
Fluids—As tolerated high in Carbohydrate	Fluids — Minimum of 3000 cc. by mouth **Diet** — High in Protein and Carbohydrate
Continue Oxygen as indicated	
Enema	Enema — Q. 2 days P.R.N.
t	
ris,	
No dressing change	No dressing change
ing ulsion	
Continue Hematocrit, Hgb. and Plasma Proteins Q. 4 H.	Continue Hematocrit, Hgb. and Plasma Proteins daily as indicated Blood count daily
Blood Chemistry Plasma Proteins Chlorides Sugar Sulfonamide Level	**Blood Chemistry** — Sugar, Urea and Creatinine if indicated by Toxemia or Urinary Suppression Sulfonamide Level if necessary
Uranalysis	Uranalysis daily
T.-P.-R. Q. 4 H. B.P. and P. Chart Q. 1 H. Hematocrit, Hemoglobin and Plasma Proteins	T.-P.-R. Q. 4 H. B.P. as indicated Hematocrit, Hemoglobin, Plasma Proteins
Intake and output daily amount all types of infusions separately in units	Intake and Output Plasma and all other infusions, sulfonamides and progress notes

ATMENT OF MAJOR BURNS

PERIOD	GRANULATION PERIOD 6th to 14th Day	HEALING PERIOD 2nd to 6th Week
h Day ates	Codeine or Barbiturates when indicated	Codeine or Barbiturates when indicated
or intravenously not desirable especially if urine volume day		Sulfonamides only indicated orally if pneumonia threatens
s indicated	**Fresh Blood Transfusions** at least 500 cc. Q. 3 days, and depending on R.B.C.	**Fresh Blood Transfusions** at least 500 cc. Q. 3 days, and depending on R.B.C.
by blood	Infusions if indicated	
od chlorides		
3000 cc. by	Fluids — 3000 cc. daily	Fluids — 2000 cc. daily
in and	**Diet** — Controlled by Blood Chemistry	**Diet** — Same Tube Feeding if necessary for Hypoproteinemia
	Vitamins and Iron	Vitamins and Iron
.R.N.	Cathartics as indicated	Cathartics as indicated
	Superficial Burns (1st and 2nd°) Remove dressing on 8th to 10th day because healed as a rule	**Superficial Burns**— Usually healed. No dressing
	Deep Burns (3rd°) Redress and remove débris on the 12th–14th day	**All Deep Burns.** Change every 12 to 14 days
	Anesthetic if necessary	
	Graft as soon as possible	**Grafting** at each change
	Homografts if necessary	
	Occlusive pressure dressing in all cases, including donor areas	**Occlusive pressure dressings in all cases, including donor areas**
Hgb. and as indicated	Continue Hematocrit, Hb. and Plasma Proteins daily as indicated Blood count daily	Hemoglobin and Red Blood Count and Plasma Proteins at least twice weekly
Sugar, Urea and d by Toxemia or	**Blood Chemistry**	**Blood Chemistry** — as indicated Sulfonamide level if necessary 3 days
ecessary	Culture with dressings	Culture with dressings
	Uranalysis Q. 2 Days	Uranalysis
	T.-P.-R. Q. 4 H. B.P. as indicated	T.-P.-R. Q. 4 H. B.P. as indicated
in, Plasma	Hematocrit, Hemoglobin, Plasma Blood Counts Proteins daily	Hematocrit, Hemoglobin, Plasma Blood Counts at least twice weekly Proteins daily
ama and all other es and progress	Same daily including blood transfusions Notes on granulation and operations	Notes on granulation and operations

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GROUP (A)—BREAKDOWN ACCORDING TO AREA OF BODY SURFACE BURNED

Ten per cent of Body Surface. Twenty of them were 10 per cent or under, but are included for certain specific reasons, *e.g.*: (a) Their particular location involving hands, genitals and face; and (b) because they had a pre-existing infection before being treated by this method.

Ten to twenty per cent—There were 40 cases in this group, included for the following reasons:

(a) Some were serious burn problems, and there was one death, an infant in shock.
(b) Some were skin-grafted.
(c) Some were representative of a group of superficial burns, showing rapid exit from hospital under adequate treatment.

Twenty to thirty per cent—There were 26 cases in this group. All were severe burn problems requiring antishock measures, and several were grafting problems. *There were no deaths.*

Thirty to forty per cent—There were ten cases in this group. All suffered severely from shock and to some extent from toxemia. There were three deaths: (1) A case complicated by steam inhalation, with respiratory congestion and pulmonary edema. This case died 11 hours after admission; (2) a child of three, died from toxemia on the third day; and (3) a nine-year-old child who died in 12 hours from shock and asphyxia.

Forty to fifty per cent—There was one case in this group. This case died from toxemia.

Fifty per cent and over—There were three cases in this group—two of them were 80 per cent burns. Both died—one from shock, and one from inanition, with severe psychosis. The third patient, with about a 60 per cent burn, is living and well.

GROUP (B)—BREAKDOWN ACCORDING TO DEPTH OF BURN

In discussing this series of burns according to their depth we submit our working classification, with comments. Burned skin reepidermizes (heals) from the following sources of epithelium: 1. Margin of the wound. 2. Viable epithelium remaining on the surface. 3. Hair follicles and sebaceous glands. 4. Sweat gland ducts.

The propensity for healing (reepidermization) of burned skin will depend upon the number of available sources of epithelium for regeneration.

Number 1 is always available but, of itself, in all but burns of small area, is insufficient for good results.

Numbers 1, 2, 3 and 4 are all available only in superficial burns.

Numbers 1, 3 and 4 are available in burns which destroy the epidermis but do not extend deep enough to destroy the hair follicles.

Numbers 1 and 4 only are available when destruction extends beyond the depth of the hair follicles but does not reach the sweat glands.

Number 1 only is available if there is full-skin destruction, or deeper.

In the average burn Numbers 3 and 4 (hair follicles and sweat gland

ducts) play a very important rôle and, since these structures vary greatly in number and depth of location in the skin in different parts of the body, so the available sources of regeneration of epidermis will vary with the locality involved.

If both hair follicles and sweat gland ducts are available reepidermization, under optimum conditions of treatment, will probably be rapid and satisfactory.

If sweat gland ducts alone are available, reepidermization will be very slow and, by the time it is complete, there would have developed abundant granulation tissue with organization into fibrous tissue and an end-result of scar skin. Exceptions are the palm and sôle, where sweat glands are very numerous and hair follicles lacking.

Superficial burns with blister formation are easily recognized. So, also, are burns which destroy the skin completely. But, in burns in which the skin is partially destroyed beyond the depth of the superficial ones, it is usually impossible, on first observation, to be certain to what depth destruction has extended. Moreover, our examination of biopsies from many burns reveals a great deal of variation in depth of destruction so that it is impossible to be certain how much epithelium has been spared for available sources of reepidermization.

For the above reasons one must let time decide whether spontaneous healing will occur, or whether it will not, and skin grafting be required. Essentially, burns may be divided into the two classes: (1) Those that reepidermize spontaneously and rapidly enough to give good results; and (2) those that will not reepidermize rapidly enough, or at all, and will require grafting.

Since there are two obvious degrees of burns, the superficial and deep, and a less obvious intermediate degree of uncertain depth, we would suggest that for classifying burns at the time of the accident, three degrees only need be used, *i.e.*, superficial, intermediate and deep. Time will split the intermediate class into two divisions—those that heal spontaneously and well, and those that do not.

Ultimately, by the aid of time, we may then for purposes of record include four degrees in our classification:

1. Superficial (down to level of papillae, usually forms blisters).

2. Superficial-intermediate (from papillary zone to a level just below sebaceous gland and sparing the lower end of hair follicles).

3. Deep-intermediate (below No. 2 and to a level above the sweat glands, in which most of the hair follicles have been destroyed).

4. Deep (from the level of the sweat glands down).

In the classification herein presented, Groups 1 and 2 healed spontaneously, and Groups 3 and 4 required skin grafting.

Many cases in Group 3 might have ultimately healed, but the process would have been long delayed, exposing the patient to the hazards of granulating surfaces over a long period of time and, at the best, healing by scar skin.

Our criteria for the divisions of the intermediate degrees is whether or not reepidermization is well advanced at the end of 14–21 days. *In the last analysis, and from a practical surgical viewpoint, every case of burn that requires dressing falls into one of two groups—those that heal spontaneously and satisfactorily, and those that do not, and should be skin grafted.*

In this series 17 of the cases required skin grafting, including one which eventually died.

Exclusive of the remaining six deaths, there were then 77 cases which healed without grafting.

Of the 17 cases that required grafting, there were four cases of full-skin thickness, or deeper, which would be classed as 4th degree, or deep, and 13 cases of partial destruction in which reepidermization was absent or would have been retarded to such a degree that healing would have occurred only by scar skin and consequent disability and prolonged hospitalization or potential fatality from exhaustion. These cases fall into our third degree or deep-intermediate.

Of the balance of 77 cases that healed spontaneously, 57 cases were easily recognizable first degree, or superficial, burns, and healed within 14 days. The remaining 20 cases fell into Group 2, or superficial-intermediate, and required an average of 22 days to heal, varying from 15–42 days.

GROUP (C)—BREAKDOWN ACCORDING TO RESULTS OF TREATMENT

GROSS STATISTICS

	No. of Cases
1. Deaths	7
2. Deep burns grafted	16
3. Deep burns not grafted (patchy areas in burns over 10%)	6
4. Superficial burns of 10%, and over, with delay in treatment of from 1-10 days, and consequent preexisting infection. Treated by a single dressing. Average time before removal of dressing 9 days. Average days in hospital, 11	22
5. Fresh superficial burns without delay in treatment, 15%-30% in area. Treated by a single dressing. Average time before removal of dressing 8 days. Average days in hospital, 10	35
6. Miscellaneous cases (burns of special areas)	14
Total	100

1. DEATHS

Case 1.—No. 5403-43: A 47-year-old male, with a fire burn of 80 per cent of the trunk, extremities, head, face, *etc.* On admission shock was very marked, with a Hb. of 130. He received 1,000 cc. plasma and 2,000 cc. glucose 5 per cent—Shock was not controlled. He died still in shock and coma at 16 hours. He received 1 cc. precortin intramuscularly.

Case 2.—No. 4402-43: A nine-year-old male had a 30 per cent burn caused by hot cinders. On admission shock was moderate (Hb. 100; B. P. 80/60). He received 750 cc. of plasma and 450 cc. 5 per cent glucose solution, but rapidly became comatose and died in 11 hours.

Case 3.—No. 8188-42: A three-year-old male child had a 30 per cent scald burn from hot water. His admission was delayed for over two hours. Shock was severe (Hb. 107; B. P. 110/70). He received 1500 cc. of plasma and 1500 cc. of glucose-saline. He recovered from shock and his condition was quite satisfactory at 24 hours. At about 28 hours, however, he developed toxic signs with vomiting, coma and urinary suppression. He died within 50 hours from toxemia.

Case 4.—No. 5328-42: A six-months-old male child, with a fire burn of 18–20 per cent from a celluloid toy, involving face, arm, forearm, hand and neck. He was admitted in marked shock and was given 500 cc. plasma plus 500 cc. normal saline. He died at 36 hours, after being apparently in fair condition with shock controlled. A few hours before death he developed edema of face, extremities, *etc.* Suppression of urine was followed by collapse, vomiting and coma. Death was apparently from toxemia. It should be noted that there was some delay in treatment. The patient was more than an hour *en route* to the hospital, and a further half hour elapsed before plasma was administered.

Case 5.—No. 965-43: A 47-year-old female, with a fire burn of over 40 per cent, who died on the ninth day in coma with suppression of urine. She had had hemaglobinemia continuously from the fourth day. Admission shock was severe but controlled. (B.P. 160/80; Hb. 114). The cause of death was not clear. The only pathologic feature, other than the burn, noted at autopsy was extensive edema of liver, kidneys and lungs. She received 3,000 cc. plasma, 2,000 cc. of whole fresh blood, 9,000 cc. glucose 5 and 10 per cent, and 1,000 cc. saline. Cortin was given intramuscularly and intravenously, but only after 48 hours.

Case 6.—No. 1625-43: An adult male of about 30 years, with a 35 per cent steam burn involving face, neck, head, trunk, arms, hands. It was complicated by the inhalation of steam and the patient required tracheotomy for edema of respiratory passages. Shock was marked (Hb. 118; B. P. 210/110). He received 1,000 cc. plasma. He died 11 hours after admission, still in shock but complicated by asphyxia from edema of the lungs.

Case 7.—No. 2473-43: A 24-year-old male who had an 80 per cent electric burn. He had been treated for 6 weeks at Arvida with compression dressings and sulfathiazole emulsion. He was transferred in a state of toxic psychosis, and refused all food. His general condition was improved with blood transfusions and intravenous therapy. He received two graftings which both took well but he died after four weeks from inanition.

RÉSUMÉ OF DEATHS

Case	Cause of Death	Area	Time of Death
1.	Shock	80%	16 hours
2.	Shock	30%	12 hours
3.	Toxemia	30%	50 hours
4.	Toxemia	18%	36 hours
5.	Toxemia delayed	45%	9 days
6.	Pulmonary congestion and asphyxia	35%	11 hours
7.	Inanition	80%	90 days

2. DEEP BURNS GRAFTED

In this series of 100 major burns treated by sulfathiazole occlusive pressure dressings, 26 skin grafting operations were performed on the 16 patients requiring grafting. The grafts were all of the delayed primary or late primary type. The cases, with significant comments, follow:

Case 1.—No. 6780-43: A 35 per cent scald in a 14-month-old female, with wide blisters and intervening white, leathery areas. Severe shock. Placed in sulfathiazole occlusive dressing within four hours of burn. Excellent recovery. First redressing on 16th day, when superficial burns were healed and the obviously sloughed areas were surgically débrided and grafted with one dermatone sheet from opposite side of the abdomen. Second redressing on 26th day, removal of sutures, 100 per cent graft take. Completely healed and discharged 30th day.

Comment: The ideal case. First redressing and grafting could have been undertaken on the 12th to 14th day.

Case 2.—No. 4736-43: Circumscribed deep burn, 8 x 6 inches, of thigh in adult male, when motor car engine was pushed against thigh in an accident. Sent in for grafting about the 35th day. Placed in occlusive sulfathiazole dressing and grafted four days later, with complete take. Discharged 14th day with complete healing.

Comment: This type of case might have had a primary graft immediately following injury and would have been in hospital 14 days only, with complete healing. Thirty-five days were wasted.

Case 3.—No. 7706-43: A four-year-old male was burned on left calf by a hot radiator. Sulfathiazole emulsion dressings as an out-patient for one month, then admitted for grafting. Area 4 x 4 inches grafted with skin from same thigh, .010 inches thick. Redressing in 13 days—complete take.

Comment: Might have had a primary graft immediately or a delayed primary graft at first redressing. The outdoor treatment should have been dispensed with.

Case 4.—Severe 12 per cent scald in three-year-old male; blisters and white, leathery areas over scapula and left arm. Admitted and placed in occlusive sulfathiazole dressing within four hours. Anxious parents refused to allow child to remain in hospital, and was treated with questionable dressing technics at home. Readmitted for grafting on 36th day. Grafted with back skin .010 inches thick on 40th day. First redressing 51st day, poor 20 per cent graft take (shoulder movement?). Regrafting was 100 per cent successful.

Comment: A poorly managed case.

Case 5.—No. 72-43: Scald, 12 per cent, in 15-month-old male child of left arm and forearm, midchest, right elbow, left abdomen and left thigh. Immediate sulfathiazole occlusive pressure dressing. Redressed seventh and 13th days; third redressing on 21st day, when all other areas were healed but thigh and abdomen, which were grafted with .008 skin from outer aspect of left thigh; fourth redressing 29th day, with 100 per cent graft take.

Comment: Too many redressings—should have been grafted earlier.

Case 6.—No. 7506-42: Deep, gasoline 20 per cent fire burn of whole left leg and buttock. Received on the 12th week, with some triple dye still adherent, infected granulations, and patient in state of inanition and low morale. Sulfathiazole pressure dressing routine. Five redressings and graftings in 70 days, blood transfusions twice weekly and at operation. Eight weeks convalescence with complete healing and no disability.

Comment: An excellent lesson in delay from eschar. This case should have been begun in the third week. All the grafting would now have been done in three operations, with two surgical teams each time.

Case 7.—No. 3309-42: Deep 20 per cent burn in 70-year-old male who was burning rubbish when paint and benzene content exploded. Grafted at third redressing on 28th day to left forearm and elbow, complete circumference. Three successive graftings completed by the 45th day.

Comment: Grafting should have been started earlier and completed in two operative stages.

Case 8.—No. 2420-42: Scald, 10 per cent, of back of thigh in five-year-old male, of which 5 per cent was a deep burn. Treated in the outdoor for three weeks and admitted for grafting. Grafted after five days sulfathiazole pressure dressing routine with 28-square inch of skin .010 of an inch thick from the midback region. Second redressing 14 days later with complete take.

Comment: The outdoor treatment should have been dispensed with and the grafting undertaken earlier.

Case 9.—No. 8122-42: Scald, 20 per cent, of chest and abdomen in three-year-old male. Sulfathiazole pressure dressings from the start. Grafted at second redressing 18th day, with surgical removal of burn slough. Twenty-eight-square inch cut from the midback region, .010 of an inch thick. Spotty 60 per cent take at third redressing, probably due to abdominal respiratory movement. Regrafted with complete take.

Comment: An unfortunate graft take, probably due to abdominal movement.

Case 10.—Flame burn, 20 per cent, from burning pyjamas in four-year-old male. Penis and scrotum burned superficially, both thighs and right lower leg deeply. Sulfathiazole emulsion routine from the start. Fourteenth day, as slough was separating, was placed in saline bath routine for 72 hours, with pain, rise in temperature and lowering of morale. Dressing routines resumed and grafted on 29th and 39th days with complete coverage and no resultant disability.

Comment: A lesson on changing treatment routine. Grafting should have been started at the 14th day, redressing instead of the change to saline.

Case 11.—No. 2888-42: Scald of thigh, knee and leg in 61-year-old female. Thigh and knee treated with sulfathiazole emulsion pressure dressing, and healed in 18 days. A gentian eschar on the lower leg became infected and would not come off. Admitted to ward, eschar removed, pressure emulsion dressing for three days. Grafted, with 100 per cent take, and healing in 12 days.

Comment: Should have been a ward case from the start. A lesson in comparative eschar and pressure dressing treatment.

Case 12.—Bed clothing caught fire burning 41-year-old male from above the iliac crest to midpart of lower leg. Pressure dressing from start. Whole leg surgically débrided on 12th day, and upper part of thigh grafted with back skin cut at .008 inches, using three good sheets. Sixty per cent take at next redressing. Burn was deeper than suspected, and whole fascia lata from midthigh down was sloughing. Redressed and grafting completed about the 50th day.

Comment: Our first delayed primary graft. It was difficult to assess the burn depth but there was a 60 per cent take of the skin grafted.

Case 13.—No. 2006-42: Ignited gasoline burn of chest and arms of 12-year-old male; 30 per cent deep burn. Chest and arms allowed to granulate for three months under triple dye eschar. Sulfathiazole emulsion and pressure dressing routine and grafting completed in two stages. Heavy scarring where skin had grown in during the three month granulation interval.

Comment: The old method of delay and wishful hoping for skin coverage. This child's illness could have been shortened at least two months.

Case 14.—Burn, 25 per cent, of leg, both hands and face from ignited kerosene in 40-year-old male. Deep burns of backs of hands grafted on the 34th day with outer thigh skin at .016 inch, with 100 per cent take.

Comment: Both backs and palms of hands and side of face subjected to same heat and only backs of hands show full-thickness burn.

Case 15.—No. 6773-43: Hot paint burn of right shin region, 8 x 10 inches, in 30-year-old male, grafted with outer thigh skin, .010 inch thick, on the 21st day. Surgical débridement before applying the graft. About 90 per cent take.

Comment: The débridement was difficult and hard to delineate in the shin area.

Case 16.—Severe, deep 30 per cent flame burn in 23-month-old male child. Immediate sulfathiazole pressure dressing routine when shock was controlled. Complete denudation of abdomen and left leg down to ankle on the ventral surface. Completely covered at third redressing using child's own back skin and two sheets of isodermal graft from the mother's buttock. Case progressing.

ASSESSING THE BURN DAMAGE

The significant features of the burn history and the clinical appearance of the burned areas are carefully assessed and provide the most reliable guides as to burn depth and the probability of skin grafting to come. A scald from moderately hot liquid producing an erythematous or lightly blistered skin will undoubtedly be a superficial burn, healed at the first redressing. A burn from excessively hot liquid or superheated steam with wide blisters and the intervening skin with a white, leathery appearance will be a deeper burn and need grafting. Flame burns as from ignited clothing are uniformly deep, the skin is seared and one may plan on its surgical removal and early grafting. Electrical burns are even more severe and often show very deep charring which may further complicate the skin grafting to follow.

In assessing the burn damage, the extent is calculated and recorded following Berkow's tables. We have discarded all previous classifications of depth, finding them confusing and of little practical value, and prefer to speak of superficial burns, which will regenerate quickly, and deep burns, which will require skin grafting.

ISODERMAL GRAFTING

Grafting of other than the patients own skin has not been employed to any great extent but we believe that this procedure may be a great help in selected cases and that more experimental work is indicated. In Case 16 it permitted the covering, in a small baby, of a very large and dangerous burn area all in one operation, two sheets from the mother and two from the child being used. Sixty-four square inches were cut from the mother's buttock and about 60 square inches from the child's own back. This permitted complete surfacing of the child's burns in about an hour's time, which is a real achievement even if the mother's grafts are only temporary. The possibilities of fetal skin and fetal skin banks might well be looked into for just such cases. The two sheets of skin almost denuded the child's whole back while the two maternal sheets made little difference to the mother's buttock.

INFECTION AND GRAFTING

With the sulfathiazole occlusive dressing there has been no cross-infection and *Streptococcus pyogenes, Bacillus pyocyaneus* and *Bacillus proteus* have been notably absent. As these organisms are the great destroyers of skin grafts, their absence has been most welcome. *Staphylococcus pyogenes* and nonpathogenic skin organisms have been culturable from our wound surfaces but seem to be in an attenuated state, certainly not producing clinical infection, or if so, to a very limited degree. We consider them no contraindication to skin grafting.

GRANULATIONS AND GRAFTING

Skin grafting of the burned surface is preferable before granulations become manifest. Exuberant granulations are an abortive attempt at wound healing that has been unsatisfied by skin covering at the appropriate time. They are the result of prolonged wound treatment and are no serious contraindication to skin grafting, *provided they are removed.* We have preferred to remove them, scraping them down to a firm yellow base with a sharp scalpel, grafting at once, feeling this procedure preferable to applying surface medicaments or lotions in an effort to make them more acceptable. A skin graft does well on the granulation tissue base but may do poorly on the granulations. There is less bleeding if they are scraped rather than cut and the resulting base is more even. The skin graft is applied immediately and itself has a marked hemostatic effect on the numerous small bleeders.

THE CHOICE OF DONOR SITES

The Padgett dermatome makes most body surfaces available for skin. The skins of abdomen, chest front, bicipital region and inner thigh are thin, and our preference has been for the thicker, better texture skin of the

back or loin regions. Outer thigh skin is midway between in quality and this site is most handy and accessible. Our abdominal and lower front chest donor sites have healed poorly compared with the other sites. We feel this is due to the difficulty of restricting the respiratory movements in these areas and that the pressure dressing is here less effective. Our donor sites are dressed in identically the same way as the original burn and the dressing left for at least two weeks or longer, until it practically falls off. Early removal is liable to damage a reforming epidermis. The donor sites are not, if possible, redressed and brought out into the air with vaseline or olive oil massage.

TIME OF GRAFTING

We prefer, if possible, to graft at the first, second or third redressing, and rather the first than the third. This may entail, and usually does, surgical removal of the damaged burn tissue but this is no more than the old method of surgical débridement, only done at a better and controlled time, both as regards the patient's general and local condition. It is simply débridement on the tenth to 14th day and covering the wound with a dressing—the skin graft. This is a delayed primary graft, the usual type. An immediate primary graft may be done on selected, circumscribed, obviously deep burns in which there is no threat of shock or toxemia.

PREPARATION OF THE BURNED AREA

We wish to emphasize the fact that with the technic advocated no other preparation of the burned area for grafting is necessary than the removal of the dressing and subsequent débridement of the area intended for grafting.

DEEP BURNS NOT GRAFTED (6 CASES)

There were six cases of 10 per cent burns, or over, that had patchy areas of intermediate deep burn which were not considered extensive enough to necessitate grafting. None of them was severe enough to threaten life. These cases were all treated by multiple, infrequent pressure dressings with sulfathiazole emulsion, changed at from seven- to 14-day intervals. Their average healing time was 24 days, the longest being 40 and the shortest 18 days. *None showed evidence of invasive infection, and epidermization was rapid and progressive.* This is the point desired to be brought out in discussing this group *but it is equally applicable to all the other groups.*

BURNS WITH PREEXISTING INFECTION

In this series there was a group of 22 superficial burns showing clinical evidence of infection on admission, as a result of delay, neglect or unsatisfactory self-treatment. The time-lag between the burn and hospital care

varied from one to 17 days, the average being five. The preliminary treatment, self-inflicted, or otherwise, varied from nothing to tannic eschar, while sodium bicarbonate, boracic and saline compresses were common. Cod liver oil had been used in three cases. In all of the cases there were local signs of invasive infection and eight had definite lymphangitis and adenitis. All of the cases showed fever and this was quite high in several. Cultures from the burned areas yielded both pyogenic streptococci and staphylococci in most instances. In all but two instances a single compression dressing sufficed to produce control of the infection and healing. The two exceptions had two dressings each. One of them is illustrated in color in the original paper.[1] The point to be brought out in this group-study is that saline baths and other types of local therapy are not essential for such cases. On the contrary, the sulfathiazole emulsion under the occlusive compression dressing was adequate. Oral sulfonamide therapy, advocated by some authors[2] as necessary for control of infection in burns, was not used in any of these cases. It may be argued that oral therapy should have been used in the presence of lymphangitis. With this viewpoint we will not take issue, and it may be advisable at times. We did not use oral therapy in order to avoid confusing the issue. The average period of time of the single dressing in these cases was nine days, the longest being 17 and the shortest five days. The average number of hospital days was 11, the longest being 21 and the shortest seven.

FRESH SUPERFICIAL BURNS (35 CASES)

(Contaminated but apparently not infected).—Thirty-five cases of superficial burns from all causes, involving over 10 per cent of various parts of the body have come under treatment within a few hours of the accident. The average time-lag between burn and treatment is over an hour. Several, however, were from four to six hours before admission. Just as in the case of wounds, these burns are presumed to be contaminated, though on admission there was no evident infection. The average area burned in these cases was 20 per cent, and six were between 25 and 30 per cent. Consequently, many were serious burn problems. The flash or explosive type of burn involving both upper extremities, face, head, neck and part of chest is typical of this group. This has been found to be a common industrial type of burn. Most of the cases were in moderate to severe shock and required antishock general treatment. Under such controlled measures nearly all responded so well that plasma could be discontinued after 24 hours. Several subsequently showed definite signs of toxemia but it is noteworthy that only one of this group died, an infant of six months who became comatose and anuric quite suddenly, in 30 hours, and died 36 hours after admission.

Our conception of these cases is that they must all be regarded as severe '*wounds*,' with necessary antishock measures to be taken before dressing

them. The amount of plasma administered on the average 20 per cent burn was rather less than we anticipated. A single dressing sufficed for the local treatment of all of these cases. It was removed in the average case on the eighth day, the shortest time being six days and the longest 15. The average number of days in hospital was ten, the shortest being six and the longest 18. Again it should be pointed out that oral sulfonamide therapy was not used in any of these cases.

MISCELLANEOUS CASES

Fourteen miscellaneous cases are included as a group in this series. They are grouped as such because, for one reason or another, they did not fall into the other five groups. Among the reasons may be noted the following:

(a) Eight of them were under 10 per cent of body surface but involved special areas, and were considered severe enough problems to be hospitalized. This lot included four burns involving the face, ears and eyelids. These averaged only 5 per cent but special complications were feared, though they did not materialize. The four others involved one or both hands and forearms and were considered to be fairly deep burns. All eight cases eventually healed without grafting and with, at most, two dressings. The average time in hospital was ten days, the shortest being six days and the longest 18.

(b) The other six cases were 10 per cent, or over, superficial burns who had involvement of special areas such as buttocks and anal region, scrotum, labia, and one of both feet (rare). They mostly presented the problem of special and more frequent dressings. In such areas as scrotum, labia, anal region or perineum it is obviously difficult, if not impossible, to apply a satisfactory compression dressing. In such areas the emulsion has been used as a cold cream on gauze dressings held in place by T-binders and changed when necessary to toilet properly. While it is impossible to maintain the same degree of noncontamination in such cases, the burned areas were kept remarkably clear and healed well without grafting. The average number of hospital days was 12, the longest being 21, the shortest ten. None of this group received oral sulfonamide therapy.

COMMENT: Without exception, all of the 100 cases in this series have been treated according to the plan suggested in the original paper. However, accumulated experience has caused the adoption of certain minor modifications. This evolutionary effect is only natural, as increasing experience has led to crystallization of thought. The planned management may now be said to have matured further. Additional improvement in any such system may be expected, and is naturally hoped for. A study of the Operational Chart, in comparison with the original, will show in detail how this progress has been effected. The principal changes may now be discussed briefly.

The most significant change to be noted is the elimination of all reference to eschar therapy. This has come about as a direct result of our knowledge that such therapy definitely obstructed the plan for early grafting of the deep burns, and that in more superficial ones the further destruction of skin, with

or without infection, caused such delay in healing as to make eschar therapy undesirable. All this quite apart from the argument regarding the toxicity of tanning agents, and other undesirable or questionable features. When compared with our experience in previous years with eschar therapy, the compression dressing has given so much better results that the former has now no recognized place in our burn management.

Regarding the "timing" of dressing change, we have found that, contrary to our early impressions, weekly or earlier redressing was undesirable. We now believe that the frequency of dressing depends upon the depth of the burn and whether grafting is to be anticipated, or not. Thus, in all obviously superficial burns, a single dressing for a week will suffice, and it would be superfluous to keep the dressings on longer. Therefore, in such cases, *i.e.*, flash burns, we follow the foregoing rule. In deeper burns, on the other hand, it is unnecessary to remove the original dressing until from 10–14 days, when débridement of the surface may be carried out and grafting commenced at once. Longer periods for the original dressing have been found unnecessary. Burns of the face, originally treated with a cotton mask, have now been found to be particularly adaptable to a compression dressing. Under this treatment there is less edema and healing is more prompt.

MANAGEMENT OF SHOCK IN BURNS

The early recognition of oncoming shock and its prompt treatment are of prime importance in the management of burns. It is generally admitted that hemoconcentration due to loss of blood plasma from the effective, or circulatory blood, is encountered in extensive burns.

A study of the cases in this series indicates that other factors may contribute towards its production. Shock in burns can, and does, exist in the absence of hemoconcentration, as determined by hemoglobin and hematocrit determinations. Let us take for example the case of No. 4402-43, a nine-year-old boy, with a 32 per cent burn from hot cinders. Six hours after receiving his burns he was obviously in shock; cyanosed, sweating, with unobtainable blood pressure and pulmonary edema, yet the hemoglobin was 92 per cent, the R. B. C. count 5,000,000, and the hematocrit value 45 per cent—perfectly normal values. Three hours later the hemoglobin was still within normal limits (80 per cent) although the hematocrit value had risen to 59 per cent, indicating severe hemoconcentration. In point of fact, shock in this case, we believe, was aggravated by a long surgical débridement carried out without anesthesia other than morphine, and was subsequently aggravated by hemoconcentration. In other cases loss of plasma proteins with replacement by crystalloids may precipitate shock in the absence of evidence of hemoconcentration.

It is manifestly impossible to predict on a clinical basis what factors, or combination of factors, are operating to produce shock in any given burned patient. The prevalent belief that a burn of a given area requires so many

liters of plasma to combat shock may be a good working hypothesis and of practical value where facilities for proper blood studies do not exist but it is not always sound therapy. When hemoconcentration does not exist, the too liberal use of plasma may result in edema of lungs, liver and kidneys, the only pathologic change noted in one of the fatal cases in this series. When possible, every extensive burned patient should be subjected to determinations of plasma proteins, hemoglobin and hematocrit estimations at two-hour intervals during the initial period and later if the shock seems imminent.

The type of therapy—whole blood, plasma or crystalloids—must be determined by the abnormalities which actually exist in each specific case. Likewise, the amounts to be employed should be judged solely on the basis of the degree of the losses in each instance, and by the promptness and completeness of the response. Overenthusiastic or improper type of therapy may be fraught with as much danger to the patient as if he were not treated at all. Fear, pain, chilling, loss of plasma proteins, as well as hemoconcentration, are factors of importance in the combating of shock in burns, and they must all be treated with due regard for the variables in individual cases.

Regarding the use of electrolytes for the patient in shock, we have, for over a year now, been strictly conservative in the use of 5–10 per cent glucose solution in order to prevent edema of both tissues and vital organs. Normal saline with its added risks of edema and sodium poisoning is prohibited except where biochemical examination shows a definite depletion.

SULFONAMIDE THERAPY

It is the belief of the authors that the most important feature of the local therapy is the surgical treatment and cleansing of the burns, followed by the application of the occlusive compression dressing. This brings the burn treatment into direct line with the surgical treatment of all other fresh trauma. Nevertheless, our experience has given us the profound impression that the addition of 5 per cent sulfathiazole in an oil-in-water emulsion gives an important additional factor of safety against invasive infections as well as providing a medium for adequate curtain drainage. The use of a wide 1–2-Mm. curtain-mesh as a basic dressing is, we feel, a necessary and important adjunct to the bulky dressing. Two particular experiences have contributed to confirm our belief: *One is that we have not in a single instance in this series been embarrassed by the development of clinical evidence of invasive infection. The second, and more important experience, has been the control of preexisting infection simply by the standard treatment with sulfathiazole emulsion locally applied.* While our belief is expressed in this way we have used sulfadiazine orally or intravenously in three severely burned cases in whom pulmonary infection was suspected. Two of these cases are included in the deaths, and the third case proved to have a severe bronchitis which was controlled. We have not had

any frank pneumonias but feel that when such intercurrent respiratory infections threaten oral or intravenous sulfadiazine should be given. Apart from such cases the authors believe that, other considerations aside, the early use of these drugs in severe burns carries a grave, unnecessary additional risk to the liver and kidneys at a time when toxic manifestations from the burn itself are imminent.

To recapitulate, the oral dosage necessary to maintain a satisfactory tissue and serum level in the burned area is a menace to a severely burned person. Such is our feeling, and our experience, with the local use being so satisfactory we can see no object in putting an additional load on potentially damaged vital organs. Reference to our original paper will give the reader the results of local tissue concentrations upon which studies our conception of the rationale of local rather than oral or intravenous therapy is based.

ANEMIA AND HYPOPROTEINEMIA

The management of the severely burned patient must include therapy to combat protein and hemoglobin loss. In extensive burns this depletion is progressive and unless adequate replacement measures are instituted, may become a serious threat to life. At least it may do much to prejudice recovery and to prolong convalescence.

Hemoglobin loss should be corrected by the transfusion of whole blood, the best infusion fluid after the initial emergent period. The amount of whole blood used must necessarily be determined in each case by the erythrocyte count and hemoglobin estimation as determined from day to day. Iron in the form of Blaud's mass 4 Gm. daily per ora is well tolerated after the initial period of shock and toxemia.

Plasma proteins may be maintained either by the intravenous infusion of whole blood, plasma or other proteins suitable for intravenous use. Blood substitutes such as gelatin, isinglass, *et cetera*, may be of value as emergency measures, but they are inferior to whole blood in treating burn patients after the first 48 hours. Occasionally it may be necessary to maintain this intravenous therapy for a much longer period. This was amply demonstrated by Lund[2] in the Boston disaster report. As a rule however, the oral administration of protein is preferable to its intravenous use unless that protein be whole blood or plasma. High protein feeding is essentially the treatment in the later stages of severe burns when it is difficult to maintain normal levels. If the oral intake be insufficient, complementary intravenous amino-acid preparations should be employed. Frequent estimations of the plasma protein are obviously necessary.

The important role of early skin-grafting in the conservation of protein and hemoglobin is already discussed in this report.

BURN TOXEMIA

We are unable to offer any summary or comment on burn toxemia. We are convinced that toxic manifestations during manifest shock present a

grave risk in all severe burns. In our opinion, this unsolved problem deserves more serious consideration and research than it has hitherto been given. There are probably many toxins involved and until more data are available on their characters adequate measures for prevention and treatment are not possible. *Is this not the remaining major problem in a severely burned patient?*

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REFRIGERATION ANESTHESIA IN SURGERY*

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ALLEN,[1] in 1941, was the first to demonstrate clinically that a tourniquet could be applied to a limb and that the part distal to the tourniquet could be enveloped in ice to produce after a suitable period of time surgical anesthesia. Not only was anesthesia complete but subsequent operation could be achieved in a bloodless and practically shockless field. This method of refrigeration anesthesia, it soon became apparent, was particularly suitable for leg amputations in extremely poor-risk patients suffering from diabetes or arteriosclerosis. During the past two years numerous clinical applications of refrigeration anesthesia have been suggested, and considerable experimental work has been done in an effort to augment our understanding of this novel technic. All authors have implied, however, that many aspects and uses of this method are disputatious, and have encouraged further reports of clinical experiences with its proposed applications. We have recently had two unusual and interesting experiences with refrigeration of limbs. These cases were followed with interest by the members of our surgical staff, and they were managed with the view in mind of trying to clarify by clinical research a few of the polemical aspects of refrigeration anesthesia.

SUMMARY OF CASE REPORTS

Case 1.—Clinic No. 82438: L. M., white, female, age 52, had a long history, with numerous hospital entries for chronic pyelonephritis, with a ureteral stricture, diabetes mellitus, and obesity. She was being observed on the Gynecologic Ward for her pyelonephritis at the time of present admission. At 5 A.M. July 17, 1942, she was seized with a sudden severe pain in her left leg. The leg rapidly became cold and motionless. We first saw her at 1 P.M., approximately eight hours after the onset of pain. The entire left lower extremity was cold, hard, white, and motionless. Sensation was markedly diminished, but spontaneous pain was considerable. Femoral, popliteal, and both pedal pulses were absent. The right lower extremity was normal. She was not fibrillating, nor had she been at any time to our knowledge. Clinically, her heart and lungs seemed clear. Electrocardiograms in 1937 and 1941 were normal, but that made on July 20, 1942, showed abnormal T-waves with left axis deviation.

A diagnosis of femoral artery occlusion from an embolus was made. Papaverine, 50 mg. intramuscularly, and lumbar sympathetic block with 2 per cent novocaine failed to relieve her pain or increase the warmth of the extremity. Femoral embolectomy was decided upon, and carried out 11 hours after the onset of her difficulty.

Under 1 per cent novocaine anesthesia through a longitudinal incision crossing Poupart's ligament, the common femoral artery and its deep and superficial branches were exposed. The common femoral was occluded by an embolus, 2 cm. long by 1 cm.

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wide. Pulsation was present in the common femoral artery above the embolus but not in the superficial or deep femoral branches. The embolus was removed from the common femoral artery, and large static thrombi sucked out from both the superficial and deep femoral arteries by an oiled catheter. Mild back-bleeding was finally obtained from both the superficial and deep femoral arteries; but neither of these vessels pulsated after closure of the incision in the common femoral vessel. The common femoral vein was not ligated.

Postoperatively she was given heparin by continuous intravenous drip, and also dicoumarin by mouth. She had an embolus to the right radial artery on the first post-operative day; but the hand remained warm. By the third postoperative day the circulation obviously had not been restored to the left lower extremity, and a line of demarcation separating warm from cold, dying tissue could be felt just above the knee. On the fifth post-operative day it was decided to cool the left lower extremity in an effort to reduce its metabolic requirements for viability. We hoped we might be able to preserve the limb while collateral circulation was becoming established.

From July 22 to August 5, 1942, a cradle covered with ice-bags surrounded the left lower extremity. The thigh was maintained at an approximate skin temperature of 18° C. and the leg at 8° C., the leg being colder because of its poorer circulation. No tourniquet was applied to the thigh. True gangrene of the limb did not occur, infection did not appear, but the limb was obviously not viable for all sensation and motor power was absent. Her general condition improved, but we abandoned all hope for the limb. On August 5 a guillotine amputation was performed just above the knee under refrigeration anesthesia obtained by applying a tourniquet around the upper thigh.

Following amputation the stump was surrounded by ice-bags for several days. On the 7th postoperative day primo-secondary closure of the amputation stump was effected by tying preplaced stainless steel retention sutures. All ice-bags were removed from the stump by the 10th postoperative day, but the tissues of the stump had failed to solidly agglutinate by August 27, 15 days after secondary closure. Her plasma protein studies were normal, and vitamin concentrates had been forced during her entire illness. On August 27 at 4 A.M. she became acutely dyspneic, shocked, cyanotic with an irregular pulse approaching 200/min. Her lungs filled with bubbling râles, and frothy sputum appeared. Phlebotomy was done, oxygen and digilanid administered, but she expired shortly afterwards. Postmortem examination was not obtained. She died either from acute heart failure or a pulmonary embolus.

Gross examination of the amputated limb showed it to be gangrenous, but infection of the tissues and necrotic changes were minimal considering it had been void of circulation for 19 days. The popliteal vessel was occluded by an organizing thrombus. As soon as the thrombus was removed it was apparent the blood had not coagulated in the peripheral structures, for a radiopaque mass could be easily injected into the popliteal vessel and made to flow down the leg (Fig. 1). Even the minutest vessels of the foot were patent (Fig. 2). This raised in our minds the possibility of having saved this limb by doing an embolectomy from the popliteal artery. Refrigeration of the limb had prevented gross necrotic changes in the avascular tissues. However, microscopically, studies of the muscle, nerve, blood vessels, and skin of the amputated limb were discouraging. The muscle was completely degenerated with only sarcolemmal nuclei remaining. There was no sign of fibroblastic or muscle cell proliferation about the vessels of the perimysium or anywhere else (Fig. 3). The small vessels contained very few cells which were chiefly polymorphonuclear and appeared to be on the point of migrating through the vessel wall. The nervous tissue showed mild degenerative changes with infiltration of moderate numbers of polymorphonuclear cells (Fig. 4). The skin showed necrosis of the dermis and subcutaneous tissue with a few inflammatory cells and pigmented nuclei (Fig. 5). Mainly the epidermal papillae and a little of the deeper layers of the epidermis was necrotic. The microscopic diagnosis was gangrene

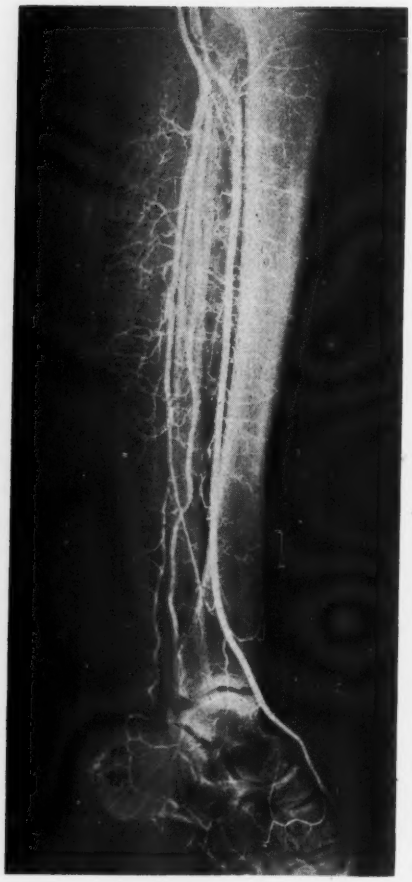

FIG. 1.—Case 1: Arteriogram of amputated leg.

of the leg. It seemed to us irreversible changes were occurring in the tissues microscopically, and that only the gross necrotic changes had been prevented by cooling.

COMMENT.—This isolated experience of refrigeration of a limb which was the seat of an unsuccessfully removed arterial embolus was not gratifying. Although cooling of the anoxic limb had retarded the metabolic needs of the tissues and prevented gross necrotic changes, we felt it had not prevented gangrene, had caused the available collateral blood vessels to contract, and had retarded both the stimulus for and rate of growth of new collateral channels.

Case 2.—Clinic No. 211107: E. M. R., white, male, age 70, was admitted to the hospital, September 16, 1942, without diabetes, but with a history of claudication in the left lower extremity for over five years. For the past seven months he had suffered in addition from an indolent ulcer on the heel of the left foot and severe pain in the calf and foot preventing sleep. General physical examination was negative except for moderate generalized arteriosclerosis. In the left lower extremity the femoral pulse was barely palpable; the popliteal, dorsalis pedis, and posterior tibial pulses were absent. The foot was cold, blanched on elevation, and exhibited dependent rubor. There was a small indolent ulcer on the medial aspect of the heel, but no gangrene of the foot or toes. He complained bitterly of pain in the foot. The right lower extremity was warmer, had a good femoral pulse, but weak popliteal and absent pedal pulses.

The pain in his left foot was so severe he insisted upon an amputation. We advised him that we might be able to relieve his pain by sectioning the superficial peroneal and sural nerves. We were particularly anxious to do this procedure under refrigeration anesthesia, and demonstrate by surgical biopsies of the nerve, muscle, skin and subcutaneous tissues any possible microscopic alterations in refrigerated tissues. Furthermore, we wondered if refrigeration would have any permanent deleterious effects on the foot after it had been allowed slowly to return to room temperature. He consented to our proposal, with the stipulation that we would amputate his leg if he was not satisfied with the results.

On September 17, 1942, a narrow rubber tourniquet was applied below the knee firmly enough to shut off the blood flow. The site of tourniquet application was chilled with ice for 15 minutes before applying the tourniquet. The leg was packed in ice and maintained at 2° C. to 8° C. for two and one-half hours. During the first hour he had moderate pain in his leg which was relieved by morphine gr. ¼. Thereafter, pain subsided and the limb became anesthetic. Operation was undertaken after two and one-half hours of refrigeration. A section of the superficial peroneal and sural nerves

was removed and, in addition, pieces of the anterior and posterior tibial muscle groups. The tourniquet was released, hemostasis obtained by fine silk ligatures, and the incisions closed.

During the ensuing four days the extremity was allowed to warm up slowly, keeping it packed in ice-bags. At first he had no pain in the leg, but after two days he began having excruciating pain of a bursting character in the entire left lower extremity below the site of tourniquet application. There was complete anesthesia over the superficial peroneal and sural nerve distributions. Gross sensation was otherwise present. He had a complete paralysis of all extensor and flexor muscle groups. His toes became blue and mottled on the 5th day, *i.e.* one day after all ice-bags had been removed.

FIG. 2.—Case 1: Arteriogram of foot.

Gangrene of his toes seemed imminent. There was no skin necrosis at the site of application of the tourniquet. The incisions seemed to be healing slowly, but because of the extreme pain and inability to move his foot he desired amputation without further procrastination. Midthigh amputation was performed under gas anesthesia September 22, 1942.

The amputated leg was examined carefully. The popliteal artery was calcified and its lumen occluded by an organized thrombus. It was impossible to inject it with radiopaque material to visualized the circulatory bed still patent. The muscular tissues above the site of tourniquet application looked normal, whereas the tissues below the site were gray, friable, and necrotic, particularly in the distal portions of the extremities. Careful sections were taken of skin, muscle, tendon, nerve and artery above and below the site of tourniquet application for detailed microscopic studies.

Figure 6 shows the normal appearing muscle after two and one-half hours of refrigeration. Figure 7 is the section of the biopsied superficial peroneal nerve, which also

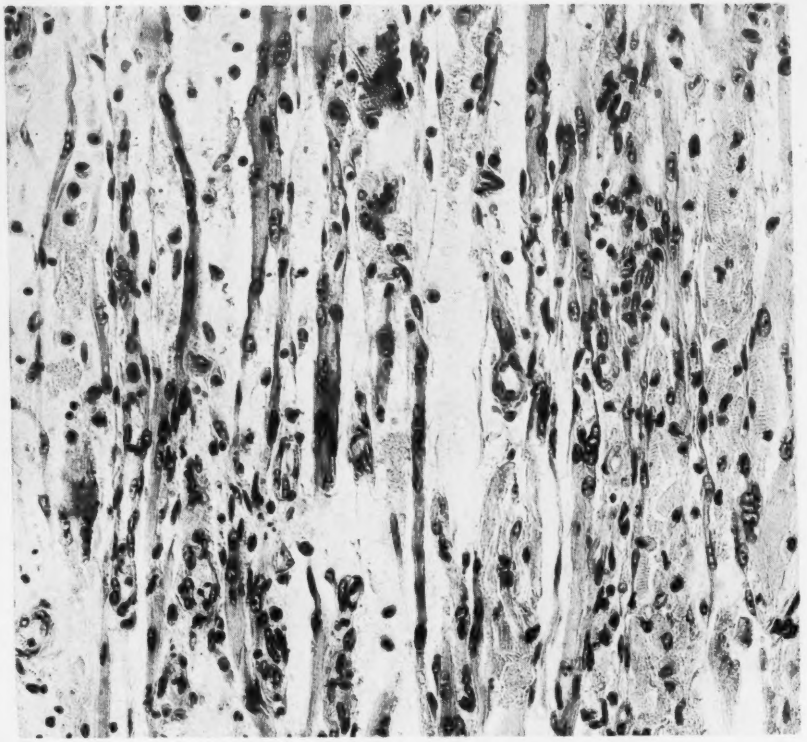

FIG. 3.—Case 1. Photomicrograph of muscle. Complete degeneration with only sarcolemmal nuclei remaining. No signs of fibroblastic or muscle cell proliferation.

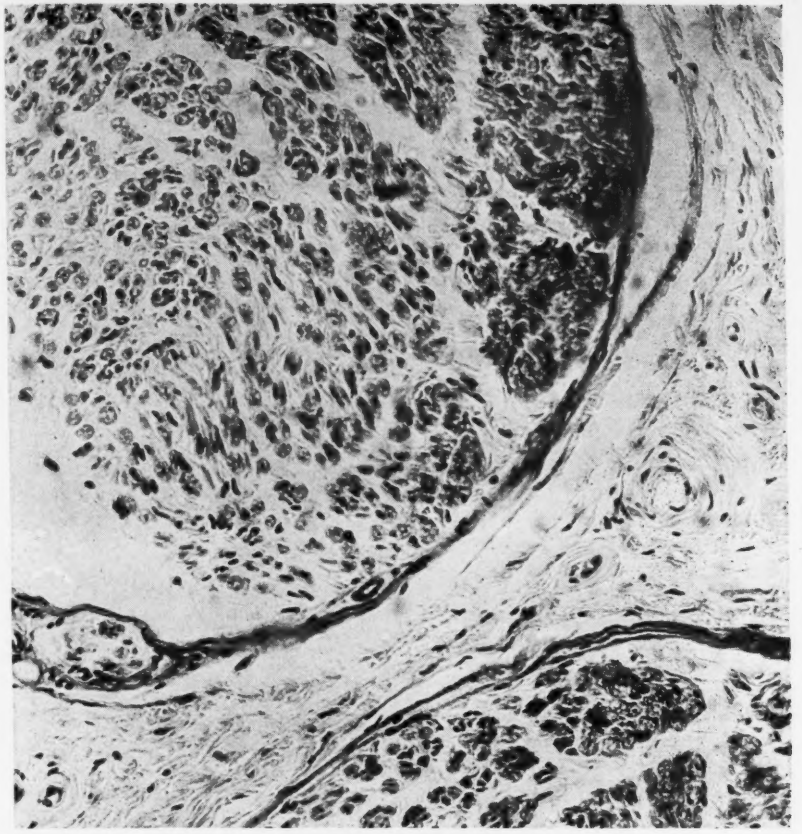

FIG. 4.—Case 1: Photomicrograph of nerve. Mild degenerative changes, with moderate polymorphonuclear infiltration.

looks normal. In Figure 8 the appearance of the muscle tissue from the amputated limb is seen. There is marked separation of the muscle fibers which have lost most of their striations. Among them are scattered moderate numbers of polymorphonuclear leukocytes and macrophages. The nerve, Figure 9, now shows a mild polymorphonuclear infiltration. Section of the skin (Fig. 10) shows normal cornified epidermis with dermis unchanged except for a few perivascular lymphocytes and moderate subcutaneous edema.

FIG. 5.—Case 1: Photomicrograph of skin. Necrosis of dermis and subcutaneous tissue, with a few inflammatory cells.

COMMENT.—To our knowledge this is the first reported case in which a limb was actually refrigerated, and then allowed to slowly return to room temperature. While it is true we were dealing with a limb which already had an abnormal circulation, we are inclined to doubt that refrigeration anesthesia may be used successfully in lengthy reconstruction operations upon normal

limbs. This skepticism would apply equally to the débridement and preservation of traumatized extremities. Once a tourniquet is applied to a limb, even though the tissues distal to the tourniquet be cooled, irreversible changes in the specialized nerve and muscular tissues are apt to occur, unless the well-established principles governing the use of a tourniquet are carefully observed.

FIG. 6.—Case 2: Photomicrograph of normal muscle after 2.5 hours of refrigeration.

DISCUSSION

In May, 1941, after several years of experimental work with the survival of tissues subjected to complete asphyxia induced by tourniquets, Allen[1] suggested, and demonstrated, the applicability of refrigeration anesthesia in clinical surgery. Briefly, the initial method of refrigeration anesthesia consisted in applying a narrow band-like (2 cm.) rubber tourniquet to the limb tight enough to obstruct all blood flow distal to it. The limb, including the tourniquet site, was encased in thin rubber ice-bags, or cracked ice, and maintained at about 5° C. until anesthesia was complete. Ordinarily, this required about one to two and one-half hours for the lower leg and three and one-half to four hours for the thigh. This method of anesthesia was designed to lower the mortality rate for leg amputations in extremely poor-risk patients, particularly in those suffering from diabetes or arteriosclerosis. The anesthesia was "protoplasmic," in the words of Allen, that is, all living

tissues and protoplasm were anesthetized, not only the nervous tissue. The operation could be carried out without haste in a bloodless field. Anesthesia lasted an hour or more, if cool solutions were used for sponging during the operation. Once the tourniquet was removed sensation returned in 15 to 30 minutes, but all bleeders could be tied and the skin closed, ordinarily with complete anesthesia. Operative shock was nonexistent because of the

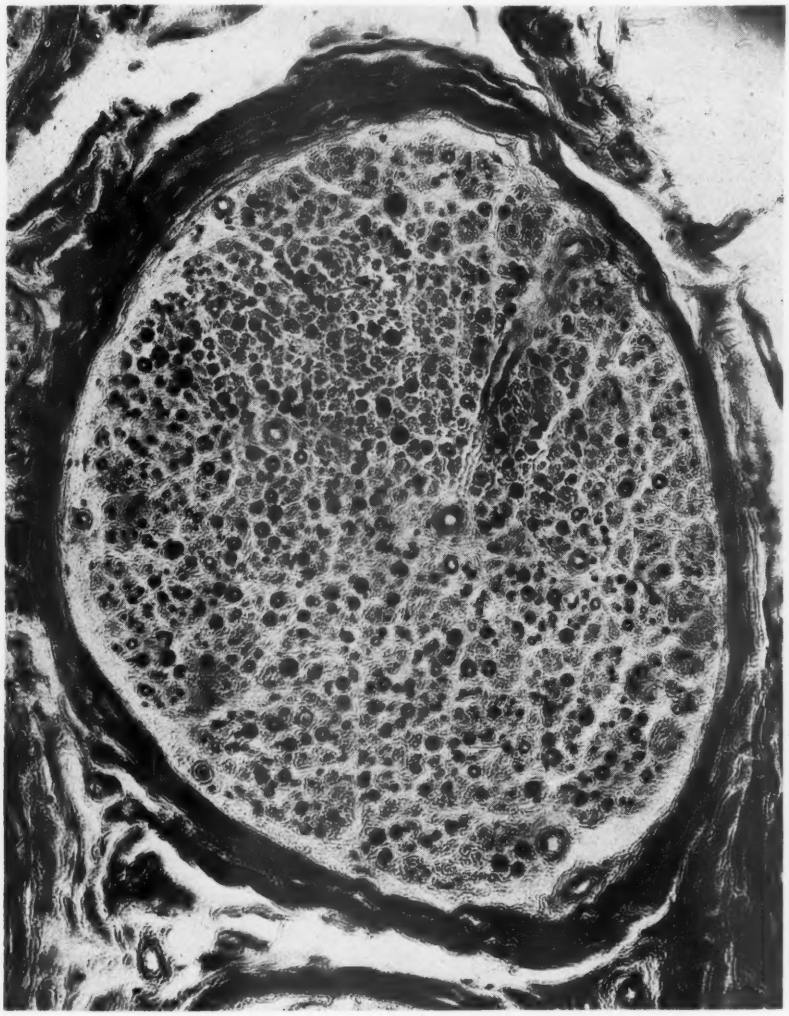

FIG. 7.—Case 2: Photomicrograph of normal nerve after 2.5 hours of refrigeration.

"protoplasmic" anesthesia. Postoperatively the stump was packed in ice-bags for several days to preserve the vitality of the flaps, inhibit shock, and prevent agglutination of the wound edges until clean healing could occur. The rate of healing was proportional to the postoperative temperature. Blood clotting and thrombosis of the vessels was prevented by cold, and emboli

from ascending thrombosis eliminated. Bacterial activity was likewise retarded by refrigeration.

Allen[1] emphasized that a tourniquet was essential to this method of anesthesia to permit chilling of the parts below it but prevent chilling of the remainder of the body. The tourniquet likewise prevents pain, shock and systemic infection from a badly traumatized, infected or asphyxiated limb. So long as the tourniquet remains in place, toxemia from the limb does not occur; but once a tourniquet has been elected for use in an asphyxiated or badly infected limb, it must not be removed until the leg is amputated, else overwhelming toxemia will ensue. Refrigeration inhibits the deleterious

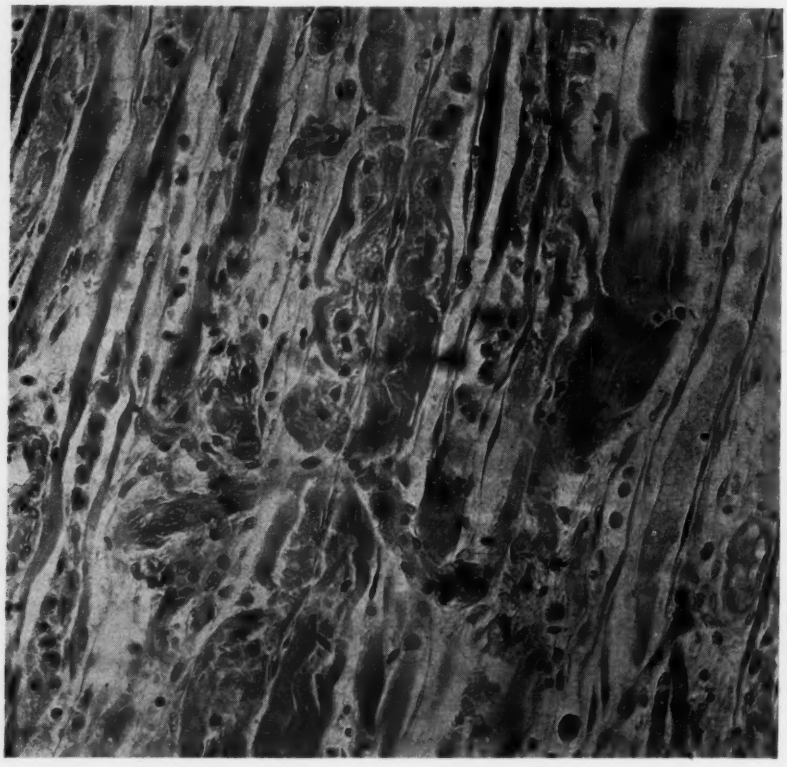

FIG. 8.—Case 2: Photomicrograph of muscle from amputated limb five days later. Marked degenerative changes with polymorphonuclear infiltration.

effects of tissue asphyxia, infection and shock proportionate to the degree of reduction of temperature. Allen advised refrigeration of badly infected or traumatized limbs in poor-risk patients until the patient could be better prepared for surgery.

In this initial article Allen also suggested other possible applications of refrigeration anesthesia might be: (1) Prevention of shock and infection in fractures, particularly those obtained in military life; (2) extension of the time limit for embolectomy with preservation of the limb by cooling until collateral circulation could develop—reduced temperatures would retard

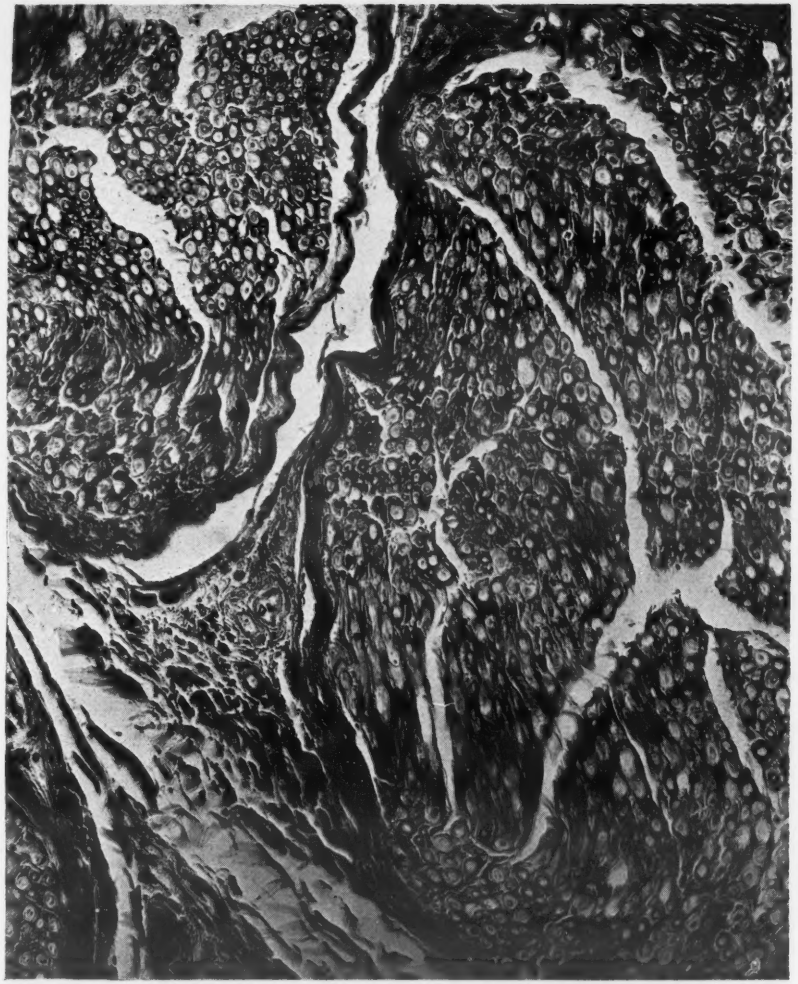

FIG. 9.—Case 2: Photomicrograph of nerve after amputation five days later. Mild polymorphonuclear infiltration.

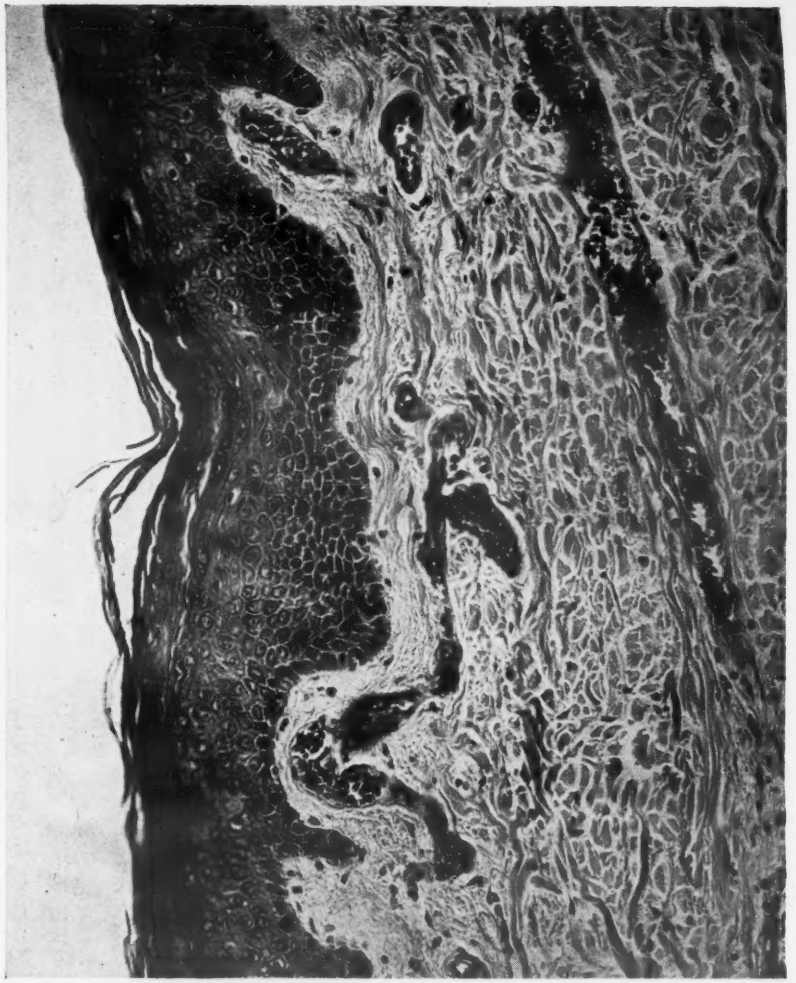

FIG. 10.—Case 2: Photomicrograph of skin after amputation. Moderate subcutaneous edema and perivascular lymphocytes. Epidermis and dermis unchanged.

thrombosis, necrosis and infection of the part; and (3) increasing the available tourniquet and shockless operative time in plastic and reconstructive procedures on limbs.

Crossman, Ruggiero, Hurley and Allen[2] were the first to report a fairly large clinical series of cases subjected to amputation under refrigeration anesthesia. An analysis of 45 cases was presented. All of the patients were extremely poor risks for amputation, suffering either from diabetes, arteriosclerosis, or fulminating infection in gangrenous limbs. Fifty-seven amputations were performed, some of the patients being amputated below the knee initially to combat toxemia, and then later having a amputation of election above the knee. There were seven deaths in this series, a mortality rate of 15.5 per cent. Twenty-one leg amputations, and 36 thigh amputations were performed. Of the 21 leg amputations, some of which were done through areas of lymphangitis, there were three deaths, and only five failed to heal; successful healing occurred in 13. Of eight reamputations at a higher level in patients initially extremely toxic from sepsis, only one death occurred. They concluded that refrigeration anesthesia occasioned the patient no pain or loss of appetite, limited necrosis and stemmed infection in a gangrenous extremity, and militated against postoperative thrombosis and embolism. They recommended the tourniquet be of pure gum rubber and one centimeter wide; that refrigeration anesthesia could be maintained for several days, permitting initial low amputations through areas of infection in extremely septic patients, with subsequent reamputation at a site of election; and that primary skin closure could be countenanced frequently in the presence of ascending lymphangitis close to the site of amputation. Refrigeration did not reduce the local vitality of tissues, weaken the barriers to infection, or create additional dangers of thrombosis or embolism. These authors used complete refrigeration with a tourniquet in all of their cases. No pathologic studies on the refrigerated limbs were offered.

McElvenny,[3] later the same year, reviewed the status of cooling of limbs in preparation for surgical procedures, and presented some additional experiences of cooling limbs without a tourniquet. He mentioned the previously suggested use of refrigeration of a limb with an acute arterial embolus, lengthening the time available for embolectomy, but stated no case reports of such a nature could be found in the literature. Two of his cases were extremely interesting. One was that of a man who sustained a crush injury with traumatic amputation of both of his legs at the knees. He was in profound shock. The stumps were packed in ice without a tourniquet for 58 hours while he was treated for shock and pneumonia and prepared for surgery. At operation, under ethylene anesthesia, the stumps were cold and firm, the muscles red and healthy, blood clots were absent, and the dirt and sand did not adhere to the tissues. Primary healing of the stumps occurred. The man suffered pain in his stumps prior to cooling, but none thereafter. The other case was that of a 78-year-old man with wet gangrene of the lower leg. His leg was kept in ice without a tourniquet

for 28 days, with no gross damage to the skin. He experienced no pain in the cooled limb. Later, a tourniquet was applied, and a midthigh amputation performed. In neither of these cases were studies presented of the pathologic material obtained. But, McElvenny concluded that cooling without a tourniquet was bacteriostatic, prevented toxic absorption, and alleviated pain in a traumatized or infected limb. He again suggested the use of refrigeration in military surgery to combat shock and hemorrhage, and slacken infection until surgery is permissible.

More recent articles of clinical importance bearing particularly on the later refinements in the technic of refrigeration anesthesia, are offered by Crossman, Allen, Hurley, Ruggiero and Warden,[4] and by Allen.[5]

It is interesting to examine the experimental observations which have induced Allen and others to express such bold convictions concerning the merits of refrigeration in surgery.

SURVIVAL OF TISSUES

Wilson and Roone,[6] in 1936 studied the effects of constriction and release of a tourniquet upon an extremity. They applied a tourniquet to the hind legs of 19 dogs under barbital anesthesia. Seventeen per cent of the control group died; all dogs whose extremity was ligated over six hours died; but all dogs ligated under three hours survived. The dangers from ligation of an extremity were: (1) nerve palsies and contractures, due either to direct pressure of the tourniquet or asphyxia of the ligated tissues; and (2) shock on release of the tourniquet. They felt the shock was due either to absorption of toxic products from the ligated limb, or to local fluid and plasma loss into the ligated extremity. They favored the latter since death was always slow and late after release of the tourniquet, and since the average increase of weight in the ligated limb was 3.5 per cent of the total body weight. (Blalock showed that 2.4 per cent of the body weight lost as plasma over a 28.5-hour period was lethal to animals.) Giving large doses of blood and plasma increased the transudation of fluid into the damaged limb, but life of the animal was lost nevertheless. Amputation alone was ineffective in saving life once local swelling had occurred in the limb, but early amputation of the ligated limb combined with large doses of blood and plasma preserved life in these animals.

Allen,[7–11] in 1938 and 1939, published several articles dealing with experimental studies on the effects of tourniquets and temperature on various body tissues. He concluded that skin and nervous tissues were most susceptible to the effects of tourniquets, and that these effects were due either to direct pressure of the tourniquet or to local tissue asphyxia. The direct pressure of the tourniquet could be tolerated by skin easily for eight hours without local gangrene. He felt the paralyses occurring after prolonged application of a tourniquet were of two types: one, direct pressure of the tourniquet on the nerve; and two, asphyxia of the nerve. The nerve would recover in several hours from the effects of local asphyxia, but not from direct pressure.

To minimize the effects of direct tourniquet pressure, a narrow tourniquet not wider than two centimeters was advised. He also found that tissues subjected to complete asphyxia would survive for much longer periods of time than commonly thought. The leg of a rat would survive, for example for 13 hours, a dog for 15 hours, and isolated examples in the literature on human limbs suggest equal resistance of human tissues to prolonged asphyxia. The main complication from prolonged ligation of an extremity was secondary shock on release of the tourniquet. This shock varied in severity depending upon the duration of ligation and mass of tissue ligated. Mild to moderate degrees of shock could be controlled by replacement of local fluid and plasma loss, but severe shock necessitated early amputation in addition to fluid, plasma and blood replacement. He postulated a toxin was formed in asphyxiated tissues which augmented the severity of shock and required early amputation of anoxic tissue prior to absorption of the toxin into the blood stream, if life were to be maintained. The toxin was liberated and absorbed slowly, for it could never be demonstrated in the blood stream, nor was the blood of a shocked animal deleterious to other animals. In addition to the general effects of tissue ligation, he discovered various tissues had different degrees of resistance and reaction to asphyxia. Nervous tissue, for instance, was most susceptible to the effects of ligation, and, even there, motor fibers were more sensitive than sensory fibers, and peripheral nerves were more resistant than the brain and spinal cord. Muscular and fibrous tissues withstand the effects of asphyxia relatively well.

Allen early noted that even slight elevation of the body temperature multiplied enormously the effects of mass ligation of tissues. Gangrene of the extremity occurred much earlier, and secondary shock on release of the tourniquet was proportionately greater. Using first the hind legs and abdomen of rats he found reducing the temperature of ligated tissue decreased the danger of both gangrene of the part and secondary shock. Later, working with rabbits and cats under light amytal narcosis, he demonstrated that by immersing the ligated limb in ice water a tourniquet could be left on the thigh for 24 to 30 hours and still have the animals survive on release of the tourniquet and allowing the limb to warm slowly. The animals had a sensory palsy for four to five days, and a motor palsy for eight to ten days; but thereafter nerve function seemed normal. He concluded that a slight elevation of body temperature, within the limits of fever, favored the appearance of local gangrene and shock; reducing the temperature correspondingly decreased the incidence of gangrene and shock. The best temperature for an asphyxiated limb was found to be approximately 2° C. On the basis of these experimental observations he postulated that refrigeration anesthesia could be used with benefit in the surgery of, (1) amputations; (2) emergency surgery, to control hemorrhage, shock and pain and permit later successful débridement or closure of wounds; (3) plastic surgery, enabling operations under tourniquets for three to five hours, or preserving skin grafts; and (4) arterial embolism or other vascular injuries, prolonging the feasible period for embolectomy

or arterial suture by avoiding intravascular clotting, and the absorption of toxins from the asphyxiated tissues.

Brooks and Duncan[12, 13, 14] conducted some ingenious experiments on the effects of temperature on the survival of anemic tissues. They determined the minimum time for gangrene to develop in a rat's tail subjected to a constant pressure of 130 mm. Hg. at temperatures ranging from −5° C. to 40° C. Between 1° C. and 5° C. the tail would survive over 96 hours, at room temperature it would survive 18 hours of pressure; but at 40° C. it survived only three to four hours. Pathologic studies on the refrigerated tails revealed, however, that even though gross survival was apparent, microscopically, there was marked fibrous tissue replacement of the muscular and nervous tissues. Another interesting observation follows: The tails of two rats were subjected to a pressure of 130 mm. Hg. at 30° C. for 16 hours, a time-period which would invariably produce gangrene. One animal was then subjected to a temperature of 40° C.; gangrene began in two hours and was marked at 12 hours. In the other, the tail was maintained at a temperature of 1° C.; the tail looked normal at the end of 24 hours, but 24 hours after the tail was allowed to return to room temperature gangrene was present. These authors offered the interesting suggestion that clinical gangrene was really a postmortem change which was readily influenced by temperature, but they wondered if tissue necrosis, of which the onset and extent cannot be clinically determined, was equally subject to temperature. They warned against the too rapid clinical use of refrigeration anesthesia. Temperature definitely effects tissue already necrotic or clinically gangrenous, but it might not alter the viability of tissue of poor viability but not dead. Cold lowers the circulation to a part as well as its metabolic needs, and many hours of refrigeration might hasten fibrosis of specialized tissues, such as nerve and muscle. They felt clinical experience was essential to answer these problems.

A recent clinical résumé by Freeman[15] on the influence of temperature on the development of gangrene in peripheral vascular disease concludes that the optimum temperature for an extremity which is the seat of occlusive vascular disease is between 30° C. and 34° C. Cold produces vasospasm; heat increases the metabolic demands of the tissues beyond their circulatory capacity, and may precipitate gangrene. Refrigeration is advised only for amputation.

CONTROL OF INFECTION BY TEMPERATURE

It occurred to Allen[16] that refrigeration anesthesia might be helpful in combating infections in the extremities. Lowering the temperature would arrest bacterial activity and application of a tourniquet would prevent the flow of toxins or bacteria from the infected limb. The inherent danger, however, would be that on release of the tourniquet an overwhelming accumulation of bacterial and tissue toxins might be released into the circulation. In one group of experiments rat feces was injected into the legs of cats and dogs. Refrigeration for two to five hours with a tourniquet had no effect on the infections. Refrigeration for 24 to 48 hours with a tourniquet

resulted in improvement while the tourniquet was in place, but on release of the tourniquet extensive masses of tissue turned dark and gangrenous and the animals died despite early and high amputations. In the second group of experiments cultures of pure streptococci were injected into the legs of rabbits. These resulted in either a trivial local process or an overwhelming sepsis, but no true cellulitis or lymphangitis comparable to human infections. Refrigeration with a tourniquet held the infection in abeyance until the release of the tourniquet, but ultimately proved of no value. Clinically, therefore, it was suggested that refrigeration of infected limbs be used to stem the infection until amputation was performed; an infected limb should not be refrigerated with a tourniquet unless amputation is contemplated. More recent clinical experiences with cooling of infected tissues will be discussed later.

Brooks and Duncan[14] studied the influence of temperature on wounds by injecting intracutaneously in the backs of anesthetized dogs oil of turpentine and *Staphylococcus aureus* cultures.

If the temperature of the wound was maintained at 40° C. there was with both the oil of turpentine and *Staphylococcus aureus* injections marked inflammatory reaction in 24 hours and central necrosis of the lesion in 48 hours. If the temperature was maintained at 10° C. only slight inflammatory reaction was present in 24 hours, and even at 48 hours gross inflammation was absent. Controls maintained at 37° C. showed slightly less reaction than the group with increased temperatures. However, after 48 hours the cooled part was allowed to return to normal temperature, and it was observed that by 96 hours the lesions resembled a control group of 24 hours. Thereafter, the lesions which had initially been cooled had slightly larger necrotic centers than the control group, suggesting cooling, in fact, irritated the tissues, resulting in a more marked inflammatory process eventually. These authors expressed the opinion that cooling inhibited bacterial growth and toxin production. The inflammatory process in the deeper tissues was not affected, for these structures were perfused by constant temperature blood. They concluded by warning against the indiscriminate use of either heat or cold on a traumatized extremity. No experiments were made on the fully developed inflammatory process.

Whereas the experimental evidence is not encouraging that cooling of an infected part has a beneficial influence on the structure, clinically refrigeration of an infected part with a tourniquet prior to amputation has proven an invaluable adjunct in controlling the toxicity and severity of a hopelessly infected limb. The clinical observations of Allen,[1] Crossman, Ruggiero, Hurley, and Allen,[2] McElvenny,[3, 17] and Haley[18] offer adequate testimony that tourniquet refrigeration of an infected limb prevents the subsequent absorption of toxic or degenerative tissue products, alleviates pain, and stems the virulence of the infection. All severely infected cases which have been refrigerated, however, have been amputated, and there are no reports in the literature of the use of cold to control infection, yet at the same time

preserve the limb. McElvenny[3, 17] has reported two cases in which cooling without a tourniquet has been practiced: (1) A 50-year-old man with traumatic amputations of both legs at the knees. The stumps were cooled by ice for 58 hours before attention to the local injuries was feasible. He felt the cooling prevented infection and preserved the vitality of the damaged stump tissues; and (2) a 78-year-old man with wet gangrene of the lower leg. The leg was kept in ice for 28 days without a tourniquet. The skin was not damaged, pain was relieved, absorption of toxins prevented, and a midthigh amputation was performed later by applying a tourniquet.

To sum the evidence up, the infection in, and toxicity from, a hopelessly infected limb can be controlled by refrigeration with a tourniquet. Amputation can then be undertaken when the patient's condition permits. Cooling, *per se*, does not seem to have a beneficial effect on an inflammatory process. While the infected part is cooled there is an inhibition not only of bacterial growth and toxin production, but also of the normal tissue response. Release from the cooling may aggravate the eventual inflammatory response.

CONTROL OF SHOCK BY TEMPERATURE

While investigating tissue metabolism and the effects of local tourniquet asphyxia, Allen[19] made some interesting observations on the secondary shock of the animals incident to the release of the tourniquet. He found applying a tourniquet to a limb was a simple, accurate, and controlled method of producing and studying shock. When the tissues of a limb had been subjected to an inadequate flow of blood for too long a period of time, death invariably resulted. This shock, which was accompanied by hemoconcentration, was felt by Allen to be due to local salt, water and plasma loss, combined with the production of a histotoxin in the asphyxiated tissues. Administration of blood, saline and plasma prevented hemoconcentration. However, after asphyxia of extensive masses of tissue, even though hemoconcentration was prevented by administration of blood, saline and plasma, death still occurred, presumably from histotoxicosis. Allen found that the effects of local asphyxia were aggravated by heat and diminished by cold. Specifically, in unanesthetized rats asphyxia of the hind leg could be tolerated at room temperature for only five hours without death of the animal, at 46° C., less than one hour, and at 2° C. for eight hours or more.

Blalock and Mason,[20] in 1941, undertook a study of the comparison of the effects of heat and cold in the prevention and treatment of shock due to either hemorrhage or trauma. Dogs under morphine anesthesia were used to study the effects of hemorrhage; morphine and ether anesthesia was used to study the effects of trauma. Hemorrhage was simulated by removing three per cent of the body weight, or approximately one-third of the blood volume, from the femoral artery over a 30-minute period. Of the 14 control animals, 5 recovered, the average duration of life of the remaining 9 being 3 hours and 33 minutes. In 9 animals heat sufficient to elevate the rectal temperature 3.7° C. was applied. All of these animals died,

the average duration of life being 5.5 hours. In 8 animals cold sufficient to depress the rectal temperature 12.3° C. was produced. All of these animals died, the average duration of life being 11.5 hours. The application of heat or cold of these degrees did not alter the chances for survival, but the application of cold doubled the survival time of the shocked animal. Comparable results were obtained when the reduction of blood pressure to shock level (75 mm. Hg.) was studied by removing blood from the femoral artery. In the traumatic shock group 8 animals were subjected to elevation of body temperature of an average of 3.6° C.; 15 animals were cooled an average of 6.6° C., as measured by rectal temperatures. The local fluid loss was about the same in the two groups. The only striking difference between the two groups were that the animals exposed to cold lived twice as long (6 hours and 35 minutes) as those exposed to heat and one of the cold animals survived. They concluded: "Significant elevations of temperature decrease the chance of life and shorten the period of survival. The application of cold does not increase the chance of survival but is accompanied with a lengthening of the survival of an animal with a low blood pressure. Significant elevations of temperature cause more disastrous effects than do depressions of similar degree."

Gratified with a satisfactory method of producing shock by crushing the hind legs of dogs in an irregular mechanical press, Duncan and Blalock[21] experimented further with the effects of plasma administration and local cold application to crushed extremities. Of the control group at room temperature that had the hind leg crushed in the mechanical press for 5 hours, 20 out of 21 died. The average survival time was 8 hours; the average increase in the weight of the crushed limb was 3.3 per cent of the body weight. Fifteen dogs had their hind leg similarly crushed for the same length of time but were given plasma in amounts equivalent to 3.3 per cent of their body weight. Nine dogs died, the average time of survival being 20 hours. The average increase in the weight of the limb was 5.33 per cent of the body weight. Therefore, two-thirds of the plasma administered was lost at the site of injury. The 6 surviving animals showed severe shock with decreased urinary output, elevation of blood nonprotein nitrogen, and plasma creatine and creatinine. The legs became swollen with yellow fluid in the fascial planes. Suppuration occasionally occurred, as did nerve palsies. Microscopically, the tissues showed extensive scarring and replacement of the muscle with fibrous tissue. In 7 animals the effects of local cooling simultaneous with the crushing were analyzed. Only 2 of these animals died, both having pneumonia. The secondary shock and local fluid loss in the injured extremity was much less, however. Six dogs had the limb crushed for 5 hours, a tourniquet was applied, and 30 minutes later refrigeration of the limb was carried out. The tourniquet was removed after 1 hour, but the ice packs were maintained for 4 more hours. All of these animals died from severe shock, and the average fluid loss in the injured extremity was 3.7 per cent of the body weight. In 5 dogs the limb was crushed only for 3.5 hours, and then treated with the tourniquet and refrigeration as above. Three of these dogs died, with an

average fluid loss of 3 per cent of the body weight and marked hemoconcentration. Marked swelling of the limb, infection with scarring, and nerve palsies also occurred. Duncan and Blalock concluded that the deleterious effects of crush injuries or traumatic shock were attributable to toxin production, and local fluid and plasma loss in the injured part. Administration of fluid and plasma prolonged life by combating these elements in shock, but did not influence the production or effects of the tissue toxin. Freezing during the crushing period protected the animal considerably from shock and local fluid loss, for the metabolism of the tissues was reduced and less injury resulted from inadequate blood supply. Refrigeration after crushing had been completed had little or no influence on traumatic shock, for anoxia had already liberated its destructive weapons.

Later work, reported by Blalock and Duncan,[22, 23] emphasized the extremely different effects between trauma alone and the same amount of trauma combined with the prolonged application of a tourniquet. Extremities were traumatized by striking the thighs of anesthetized animals a number of blows with a hammer. In one group no tourniquet was applied and plasma was administered in amounts equivalent to 5 per cent of the body weight. Every one of these animals survived. In the second group the same amount of trauma was produced, but a tourniquet was applied to the limb for five hours. So long as the tourniquet was in place the animals remained unchanged, but on release of the tourniquet death ensued despite the administration of plasma in amounts equivalent to five to 10 per cent of the body weight. From the clinical standpoint, they cautioned strongly against the control of hemorrhage by a tourniquet, and advised, if a tourniquet is imperative, to cool the part distal to the tourniquet to reduce the chances of development of shock following the release of the constriction. However, the tourniquet must be left in place as short a time as possible, unless the part is to be amputated.

A good deal of the previous experimental work of Blalock, Blalock and Duncan, and Blalock and Mason, is summarized in a recent article by Blalock.[24] Using the same experimental method for studying the treatment of shock, the hind legs of large dogs, anesthetized with nembutal and morphine, were subjected to repeated blows with a blunt instrument for five to eight minutes. Ten animals were used for each method of therapy studied. If a tourniquet was applied it was left in place for five hours. The experimental results are shown in Table I:

TABLE I

SHOWING THE ILL EFFECTS OF A TOURNIQUET AND THE BENEFICIAL EFFECTS OF LOWERING THE TEMPERATURE OF A PART DISTAL TO A TOURNIQUET

Experimental Procedures	No.	Tourniquet	Plasma (% Body Wt.)	Animals Surviving	Time Survival	Regional Fluid Loss
Trauma; plasma therapy.....	10	0	5	8	8 days	
Trauma; tourniquet; plasma.....	10	5	5 to 10	0	14 hrs.	7.8
Trauma; tourniquet; cold; plasma.	10	5	5	5	17.5 hrs.	5.42
Trauma; tourniquet; cold; no plasma.....	10	5	0	4	2 hrs. 20 mins.	5.41

Refrigeration was carried out by surrounding the limb in crushed ice, as soon as the traumatization was completed. These experiments substantiated previous work and confirmed the opinion that a tourniquet should not be applied to an injured extremity, for it burdens the patient with the harmful effects of anoxia plus trauma. If a tourniquet must be applied cooling of the part distal to a tourniquet lessens the ill effects of constricting and releasing the blood supply to an injured part. The beneficial effects of cooling of a part distal to a tourniquet may be due to a "slowing of the metabolic processes or to a number of other alterations."

TECHNIC OF REFRIGERATION ANESTHESIA

The two indispensable elements for obtaining satisfactory refrigeration anesthesia are: (1) A tourniquet applied tight enough to completely obstruct all circulation to the distal parts; and (2) ice or another mechanism for maintaining the temperature of the ischemic limb between 2° C., and 8° C. until anesthesia is complete. It must be realized that the tissues are refrigerated, not frozen. If they be cooled below 0° C., by adding salt to the ice or using other substances with a lower freezing point than water, the tissue will be frozen, and an irreversible change in the colloid structure of the tissues will occur. This freezing of the tissues or alteration of their colloidal state precludes the return to normalcy in the affected tissues. In our early experiences with refrigeration anesthesia salt was unwittingly added to the ice and sufficient care was not exerted in observing the temperature of all parts of the limb. When amputation of the leg was performed certain parts of the limb were refrigerated, but other parts were frozen. The refrigerated parts were soft, normal in appearance; but the frozen parts were hard, inelastic and solid. Fortunately, we escaped freezing of the tissues at the site for amputation in these cases.

The harmful effects of a tourniquet are due either to the local asphyxia of the structures deprived of blood or to direct pressure within the zone of the tourniquet. To minimize the local effect of a tourniquet Allen[5] recommends a narrow (1.25 cm.) band of elastic pure rubber tubing. On theoretic and experimental grounds this recommendation would apply for both the arm and leg, but clinical experience with tourniquets, in general, has induced us to favor the pneumatic blood pressure cuff for the arm. Nerve palsies occur less frequently with it than with narrow band tourniquets in the arm. In the leg, however, we have had no difficulties with the narrow elastic rubber tourniquets. This objection is immaterial if the limb is to be amputated, for skin necrosis at the site of tourniquet application is equally rare with either form of tourniquet. At any rate, for satisfactory anesthesia the tourniquet must be applied with sufficient pressure to completely obstruct all circulation to the limb.

After the site of tourniquet application has been chosen, ice-bags are applied around this site for 15 to 20 minutes to chill it. This renders subsequent application of the tourniquet almost painless. A tourniquet is then placed

around the chilled area completely occluding all blood flow distal to it (Fig. 11). If no infection is present in the limb it may first be elevated and milked free of blood by winding the extremity with an Esmarch bandage. The entire limb from the top of the tourniquet distalwards is enveloped directly in

FIG. 11.—Refrigeration Technic: After chilling of tourniquet site with ice-bags, the tourniquet is applied well above the site chosen for amputation.

FIG. 12.—Refrigeration Technic. Entire limb enveloped in ice-bags, and outer casing of rubber sheeting wrapped around limb and ice-bags.

crushed ice or in thin ice-bags containing cracked ice. Mild pain from the tourniquet may occur but this can readily be controlled by small doses of morphine. Care must be taken to refrigerate all aspects of the limb. The cracked ice or ice-bags are contained within a large rubber sheeting (Fig. 12). To prevent flooding of the bed with ice water, the head of the bed is raised and the distal end of the rubber sheeting conducts the water into a pail. If a thermometer is placed next to the skin the temperature ranges between 2° C.

and 8° C. A low thigh or midthigh amputation requires 2.5 to 3 hours of refrigeration, the upper leg 2 to 2.5 hours, the lower leg 1.5 to 2 hours. The ice is not removed until the patient is in the operating room, and the tourniquet is removed on completion of the operative procedure. Complete anesthesia lasts from 1 to 1.5 hours, depending on how careful the operator is to avoid heating of the exposed tissues. Chilled saline has been recommended for moistening the tissues and instruments.

If the amputation is to be below the knee, and the patient can sit up in a chair, the leg may simply be inserted in a bucket of ice water to obtain refrigeration. The above-described technic, though simple and effective, is rather untidy, wet, and cumbersome, and several authors have recently reported mechanical devices to facilitate refrigeration without these inconveniences. Crossman, *et al*,[2] are using an electrical refrigerator thermostatically controlled at 40° F. to obtain refrigeration, and Haley[18] has described a convenient metal cabinet to contain the limb and cracked ice during refrigeration. Haley also recommends the use of two tourniquets in infected and toxic cases, one applied during the initial upbuilding period at the tibial tuberosity, and the second applied at the upper thigh a few hours prior to amputation. This permits the area through which amputation is to be performed to be washed free of, and recover from, the effects of all absorbed toxins.

It is interesting to note that the tourniquet and refrigeration may be carried out well above the site chosen for amputation (3 to 6 inches) without fear of reducing the vitality of the tissues distally. No cases of slough at the tourniquet site or of the few inches of tissue distal to the tourniquet have been reported.

POSTOPERATIVE CARE

Postoperatively, the usual pressure dressing to and immobilization of the stump is carried out, and the stump is surrounded with ice-bags. In the ensuing 48 to 72 hours the number of ice-bags to the stump is gradually decreased, and by the 4th day no further cooling of the stump is necessary. Since agglutination of tissue fluids is retarded by cooling more serum than usual may drain from the stump, and healing is slightly slowed. Skin sutures, if used, should not be removed before the 10th to 12th day, but otherwise the stump heals satisfactorily. The degree and extent of postoperative healing can be somewhat controlled by regulating the cooling of the stump, and this is an advantage, particularly in infected cases, where too rapid healing is undesirable. Pain from an edema in the stumps is lessened by postoperative cooling.

Pneumonia is a definite complication from this method of anesthesia, particularly in the elderly, toxic, or poor-risk patients. Precautionary measures, as avoiding respiratory depression by excessive sedation, encouraging deep breathing exercises and coughing, frequent turning of the patient exercising of the arms and legs must be initiated immediately after operation.

If pneumonia or atelectasis does occur, full doses of one of the sulfonamide drugs should be administered.

SUMMARY

From an analysis of the available clinical and experimental material many of the advocated advantages of refrigeration in infection, shock, traumatic injuries, vascular occlusions and reconstructive extremity surgery seem untenable. It was hoped that refrigeration might enable us to preserve the vitality of many limbs suffering from these afflictions which would ordinarily have to be sacrificed. Bacterial growth is retarded by refrigeration but so, also, is the tissue response to inflammation, and on release of the cooling the inflammatory reaction may even be aggravated.

In an injured extremity with an intact blood supply the application of a tourniquet is extremely hazardous, for it increases immeasurably the subsequent shock by adding to trauma the effects of tissue asphyxia. It is highly questionable if cooling alone of such a limb is of value. If a tourniquet must be applied to an injured extremity, then refrigeration of the anoxic parts distal to the tourniquet will lessen greatly the subsequent shock on release of the tourniquet. Care must still be exercised to avoid prolonged application of the tourniquet if the part is to be preserved, for although gross necrosis and postmortem changes in the asphyxiated tissues will not occur the highly specialized nerve and muscular tissues in the limb may be irreparably damaged by ischemic fibrosis. The same objection to refrigeration anesthesia may be voiced against its use in extensive reconstructive operations on an extremity where a prolonged bloodless and shockless field would be desirable. Similar objections obtain in using refrigeration in the presence of vascular occlusion of an extremity. If embolectomy fails to restore the integrity of the limb, cold would have a constrictive effect on the existing collateral circulation and would probably retard the development of new collateral channels. Without a tourniquet a limb could probably not be cooled sufficiently to prevent recurrent intravascular clotting in the damaged vessel following embolectomy.

It is true that refrigeration anesthesia has decided advantages in the control of shock, hemorrhage, and infection if sacrifice of the limb has been decided upon. Clinically, this has been particularly demonstrated in elderly, debilitated patients toxic from gangrene or infection in a limb. The application of a tourniquet combined with refrigeration will eliminate the absorption of toxins, promote bacteriostasis, avoid gross necrotic changes in the limb and permit removal of the limb in a bloodless, shockless and completely anesthetic field. Herein, lies the main advantage of refrigeration anesthesia. Lower amputations are permissible, necrosis of the stump is lessened, amputation may be undertaken through a potentially infected field, and subsequent drainage of infection in and healing of the stump controlled by postoperative cooling. The dangers of spreading thrombosis or embolism are obviated. Pneumonia postoperatively, must be cautiously avoided.

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REGENERATION OF PRE- AND POSTGANGLIONIC FIBERS FOLLOWING SYMPATHECTOMY OF THE UPPER EXTREMITY

AN EXPERIMENTAL STUDY

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CONSIDERABLE CONTROVERSY exists as to the explanation of the unsatisfactory results which occasionally follow attempts to relieve vasospasm by removal of the sympathetic innervation of the upper extremity. This study aims to provide an explanation for those cases in which the symptoms reappear after a postoperative period of several months. Excluding those individuals in which the return of symptoms might be explained by an increased sensitivity of smooth muscle to epinephrine following degeneration of postganglionic fibers, the cases in which undesired results are obtained may be divided into two groups: (1) Those which show some persisting vasospasticity; and (2) those which are temporarily relieved but show a recurrence of sustained vasoconstriction after an elapse of several months.

The first group may show persistence of symptoms because of failure to remove the cervicothoracic ganglion and a sufficient number of additional thoracic sympathetic ganglia. Kuntz[3] demonstrated that, to obtain complete sympathetic denervation of the upper extremity, in many cases the second thoracic sympathetic ganglion must be resected or isolated. This was shown to be necessary because postganglionic fibers originating from cells in the second thoracic or lower sympathetic ganglia are often present in the intrathoracic ramus which extends between the second and first thoracic nerves. Kirgis and Kuntz[2] reported the presence of a smaller and less frequently occurring intrathoracic ramus between the third and second thoracic nerves. Such rami constitute a pathway by which postganglionic fibers from as low as the third thoracic sympathetic ganglion might reach the roots of the brachial plexus independently of the sympathetic trunk. Moreover, the recurrent nerves that reenter the vertebral canal contain postganglionic fibers, some of which ascend and leave the canal along nerves composing the brachial plexus (Van Buskirk[9]). Thus, these fibers constitute another pathway by which vasoconstrictor impulses may reach the upper extremity following the common operative procedures.

Several theories have been advanced in an attempt to explain the recurrence of vasospastic symptoms following temporary relief. Sheehan[4] suggested that preganglionic fibers may extend into the upper extremity to functionally replace the degenerated postganglionic fibers. However, he considered this improbable. Various workers have proposed that the return of vasomotor activity is the result of regeneration of axons whose cell bodies lie in sympathetic ganglia inferior to the usual level of trunk resection. It

has been suggested that these fibers rejoin spinal nerves to be distributed peripherally. Histologic evidence that such regeneration may occur has not yet been demonstrated.

White[10] concluded that the recurrence of symptoms in Raynaud's disease, following sympathectomy of the upper extremity, is the result of an increased sensitivity of smooth muscle to epinephrine following degeneration of postganglionic fibers. However, at the time when the relapse usually occurs hypersensitivity to epinephrine is either absent or very much reduced (Simmons and Sheehan[5]). These investigators concluded that this return of symptoms probably is due to a regeneration of vasoconstrictor fibers. Smithwick[6] states that the recurrence of symptoms following either pre- or postganglionic sympathectomy is undoubtedly due to partial regeneration of sympathectic fibers. He also suggested that recurrence of vasomotor activity may be the result of the regeneration of fibers from thoracic segments below the level of section of the sympathetic trunk.[7] This worker, in an attempt to prevent such fibers reaching ganglionic cell stations, enclosed the second and third thoracic ganglia and the intervening trunk in a small, silk sack and ligated the cut end of the lower portion of the trunk.[7]

In experimental work on cats, Tower and Richter[8] found no evidence, within 18 months, of functional regeneration of postganglionic fibers. However, they reported that preganglionic fibers regenerate within a month to make functional connections in the cervicothoracic ganglion. Evidence confirming these findings has been presented by Hinsey, Phillips and Hare.[1]

MATERIAL AND METHODS

A total of 21 cats was used in this investigation. In each instance operative procedures were performed on the right side only, the left side remaining as a control. Animals were sacrificed at postoperative periods ranging from 28 to 300 days.

Based upon the experimental procedures utilized, the animals may be divided into three groups. Group A consisted of 12 cats from which the cervicothoracic and the second thoracic ganglia were removed. In addition, the third thoracic ganglion was removed in some animals of this group. Group B included three cats in which communicating rami were extirpated. In one animal the rami between the sympathetic trunk and the second thoracic nerve were removed; in the other two animals the rami between the sympathetic trunk and the eighth cervical and first thoracic nerves were removed. Group C consisted of six animals in which a cervicothoracic and second thoracic ganglionectomy was performed and the third thoracic ganglion isolated by section of the communicating rami. The cut end of the inferior portion of the trunk was ligated and drawn into a small tube, the upper end of which was then sealed with paraffin. The tube was sutured to the prevertebral muscles. A silver tube was used in three animals and a glass tube in the other three.

To obviate possible interpretation of sensory and vagal fibers as regenerated sympathetic axons, a supplementary operative procedure was performed on several animals 10 to 14 days prior to the termination of the experiment. This consisted of extirpation of the posterior root ganglion of each spinal nerve from the seventh cervical to the second thoracic segment inclusive. In addition, a segment of the vagus nerve was resected from the upper cervical region.

Upon sacrificing the animals a careful dissection was made of the sympathetic trunk, the vagus nerve, and the thoracic and cervical spinal nerves. Connections formed postoperatively between the sympathetic trunk and the upper thoracic and lower cervical nerves were removed and prepared for histologic study. Some tissues were fixed in Bodian's No. 2 solution and stained by the protargol technic; others were prepared with osmic acid.

The extent of functional regeneration of postganglionic fibers was estimated by determining the activity of the sweat glands of the paw pads and the activity of the arrector pili muscles of the upper extremity. The function of the sweat glands was tested by the starch-iodine method; that of the arrector pili muscles by electrical stimulation of the thoracic sympathetic trunk inferior to the point of section. The extent of renewal of synaptic connections by preganglionic fibers in the cervical sympathetic ganglia was determined by the response of the pupil and nictitating membrane to electrical stimulation of the thoracic sympathetic trunk below the level of section.

OBSERVATIONS

Sympathetic denervation of the operated side was evidenced by a marked constriction of the pupil, projection of the nictitating membrane, elevation of the cutaneous temperature of the forelimb and inactivity of the sweat glands. Regeneration of preganglionic fibers was indicated by dilatation of the pupil and retraction of the nictitating membrane. This was observed in most animals by the end of the fourth postoperative month.

No indication of functional regeneration of postganglionic fibers into the upper extremity was detected by either the starch-iodine sweating test or by electrical stimulation of the sympathetic trunk inferior to the point of resection. However, the latter stimulation caused prompt and marked dilatation of the pupil in the majority of animals. Even those animals which were allowed the longest postoperative survival periods (300 days) showed, by the experimental methods used, no evidence of activity of postganglionic fibers.

Gross and microscopic examination of the sympathetic trunk and thoracic and cervical spinal nerves reveals that a rather extensive attempt at regeneration had occurred.

Removal of the posterior root ganglion of each nerve from cervical VII to thoracic II, inclusive, did not materially reduce the number of regenerating fibers. Resection of the vagus in the upper cervical region failed to modify the histologic picture.

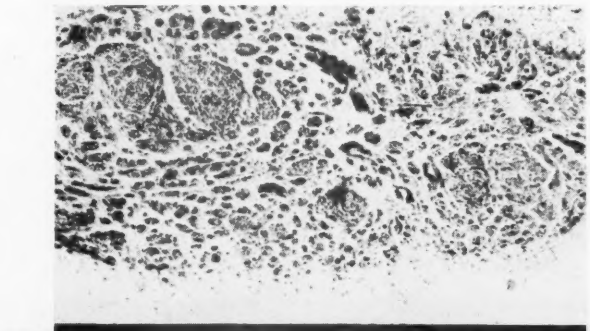
FIG. 1.—Seventh and eighth cervical and upper three thoracic nerves and sympathetic trunk six months after removal of the cervicothoracic and second thoracic sympathetic ganglia. (All photographs are unretouched)

FIG. 2.—Corresponding spinal nerves and sympathetic trunk of unoperated side from same animal as Figure 1.

In those animals in which the cervicothoracic and the second (and in some cases, the third) thoracic ganglia were removed (Group A), dissections show considerable regeneration of fibers from segments below the second and third thoracic levels (Fig. 1). The regenerating axons ascend from the cut end of the thoracic sympathetic trunk in several small bundles. Fibers which communicate with the nerves of the brachial plexus extend from these fasciculi. Many of the remaining components extend upward to the cervical sympathetic trunk, and other fibers are lost in the adjacent connective tissue. Regenerating preganglionic fibers emerge from the severed communicating rami of the upper thoracic spinal nerves and become intermingled with those axons extending upward from the cut end of the thoracic sympathetic trunk. In all cases considerable scar tissue was formed in the region from which the sympathetic nervous tissue was removed. It was demonstrated both by dissection and microscopic examination that many fibers had established con-

nections between the cut thoracic trunk and the communicating rami, which had been severed at operation. This was noted especially in relation to the rami of the sixth, seventh and eighth cervical nerves. Both the experimental (Fig. 1) and control (Fig. 2) sides present a considerably larger communicating ramus to the seventh cervical nerve than to the other nerves of the brachial plexus.

FIG. 3



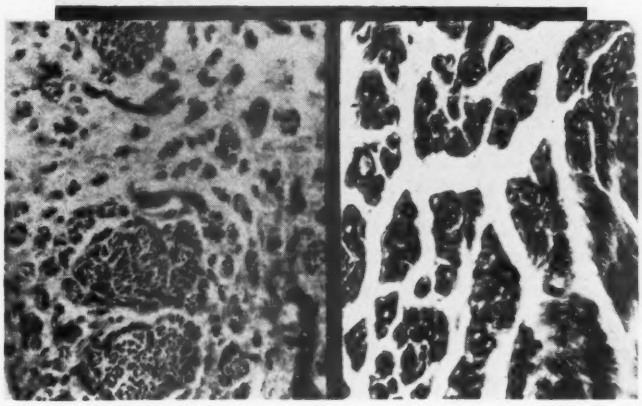


FIG. 4 FIG. 5

FIG. 3.—Transverse section of a portion of the regenerating sympathetic trunk immediately above point of section. (All photomicrographs show tissue prepared by protargol except Figure 5, in which the tissue was prepared with osmic acid.)

FIG. 4.—High power magnification of an area of Figure 3 showing thinly myelinated and unmyelinated fibers.

FIG. 5.—Area of a transverse section of the reformed communicating ramus between the sympathetic trunk and seventh cervical nerve.

Microscopic study of the bundles of nerve fibers issuing from the cut thoracic sympathetic trunk reveals many myelinated and unmyelinated axons (Figs. 3, 4, 5). There is a marked predominance of thinly myelinated axons which undoubtedly are preganglionic fibers from lower thoracic segments. The number of regenerating unmyelinated fibers varies greatly. In some instances there are more of these fibers than in the control trunk; the excess in number of fibers is attributed to branching of regenerating axons. The communicating rami between the regenerating sympathetic trunk and the spinal

nerves are composed of both myelinated and unmyelinated fibers. These fibers are not segregated, both types occurring in all communicating rami. Histologic examination of the relation of these rami to the spinal nerves reveals that many of their unmyelinated fibers course with the nerves as small discrete bundles (Fig. 6). The rami, in proximity to the spinal nerves, divide into fasciculi which join the nerves independently (Fig. 7).

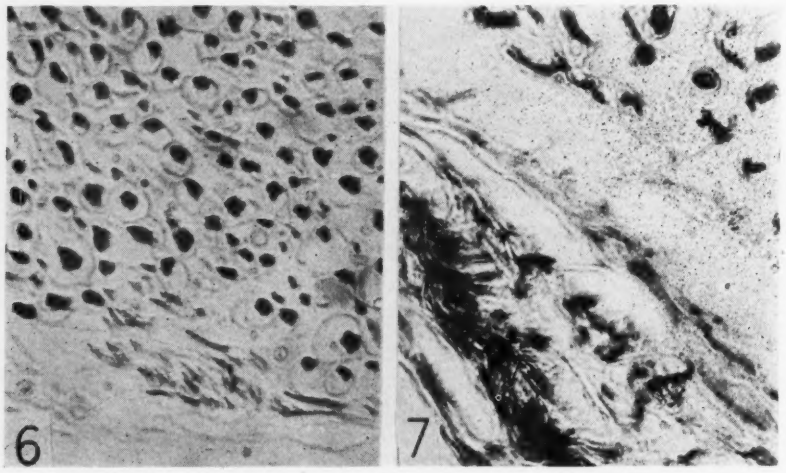


FIG. 6.—Transverse section of the seventh cervical nerve showing a small bundle of unmyelinated fibers coursing with the nerve.

FIG. 7.—Transverse section of the seventh cervical nerve showing a small bundle of unmyelinated fibers joining the nerve.

In Group B, in which communicating rami alone were extirpated, dissection shows renewal of connections between the sympathetic trunk and spinal nerves as early as four months postoperatively (Fig. 8). Grossly, these communicating rami exhibit relationships to the spinal nerves similar to those between the rami and spinal nerves of the control side (Fig. 9). Microscopically, these rami were found to consist of myelinated and unmyelinated fibers. These fibers are not as compactly arranged as in a normal ramus; instead they are grouped in numerous loosely placed fasciculi interspersed in connective tissue (Fig. 10).

In those animals comprising Group C, in which the cervicothoracic and second thoracic ganglia were removed and a tube placed over the cut end of the inferior portion of the sympathetic trunk, renewed connections were found between the sympathetic trunk and the spinal nerves (Fig. 11). The regenerating fibers emerge from the inferior end of the tube, which had not been sealed, and from that point the majority of the fibers turn and course superiorly. The number of the bundles of regenerating axons is considerably smaller than in those cats in which no steps were taken to prevent regeneration. The tube contains coiled myelinated and unmyelinated fibers and a small amount of scar tissue. In every case the tube is surrounded by a

connective tissue capsule which is penetrated by the regenerating nerve fibers. Figure 11 shows the course and character of these fibers as they reform the upper thoracic sympathetic trunk and communicating rami to the spinal nerves. As in Groups A and B, the regenerating bundles are formed of both myelinated and unmyelinated fibers.

Discussion.—It has been demonstrated that the axons of the thoracic sympathetic trunk, following section of the trunk inferior to the second or third thoracic sympathetic ganglion, exhibit extensive powers of regeneration. This is more than a mere abortive, aimless growth of injured axons. Fol-

Fig. 8.—Seventh and eighth cervical and upper three thoracic spinal nerves and sympathetic trunk four months following section of communicating rami between the sympathetic trunk and first and second thoracic nerves.

Fig. 9.—Corresponding spinal nerves and sympathetic trunk of unoperated side from the same animal as Figure 8.

lowing removal of the cervicothoracic and the second and third thoracic ganglia, thinly myelinated fibers issuing from the upper end of the severed thoracic sympathetic trunk join similar fibers emerging from the sectioned communicating rami of the upper thoracic spinal nerves to reestablish continuity with the isolated cervical sympathtic trunk. Electrical stimulation of the thoracic trunk below the operative level resulted in prompt dilatation of the pupil in most animals which survived four months or longer post-

operatively. Therefore, these fibers must have regained synaptic relation with neurons of the cervical sympathetic ganglia.

These findings emphasize the necessity of taking special measures to obviate reestablishment of functional connections by preganglionic fibers with upper thoracic ganglia when the latter are not extirpated. Our work indicates that such connections would likely be made by a rather large number of fibers. Since the great majority of postganglionic fibers which pass to the upper extremity are axons of cells of the cervicothoracic, and the second and third thoracic ganglia, it would seem advisable to remove or isolate these ganglia. However, clinical reports (Smithwick[7]) have indicated that

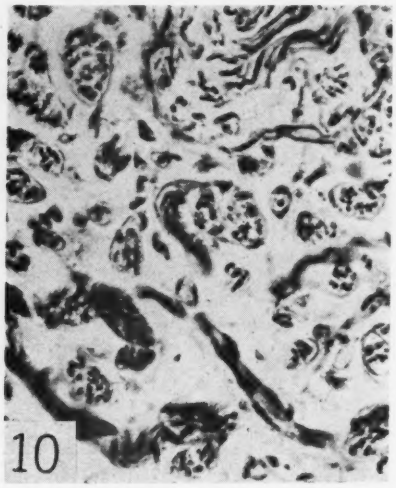


FIG. 10.—Area of a transverse section of a regenerated communicating ramus shown in Figure 8.

FIG. 11.—Seventh and eighth cervical and upper three thoracic spinal nerves and sympathetic trunk following removal of the cervicothoracic and second thoracic ganglia and isolation of the third thoracic ganglion in a small glass tube.

more favorable results are obtained if the postganglionic fibers are, insofar as is possible, allowed to remain intact. The procedure which has been recommended as giving most satisfactory results consists essentially of severing the sympathetic trunk immediately inferior to the third thoracic ganglion followed by extensive removal of preganglionic fibers of the second and third thoracic segments and isolation of the second and third thoracic sympathetic ganglia by enclosing them in a small silk sack.[7] Our observations stress the necessity of preventing preganglionic fibers of lower thoracic segments from reestablishing synaptic connections in the isolated upper thoracic ganglia.

Unmyelinated axons accompany the preganglionic fibers which emerge from the cut end of the thoracic trunk. Numerous fibers of both types extend into the surrounding connective tissue and prevertebral muscles and

thus fail to reach a spinal nerve or sympathetic ganglion. Although many unmyelinated fibers join spinal nerves, experimentation reveals no functional activity of postganglionic neurons in the sympathectomized extremity. This is in accordance with the findings of Tower and Richter,[8] who report no functional activity of postganglionic fibers in the upper extremity of cats within 18 months after sympathectomy. If functional connections are reestablished by these fibers, as has been reported clinically, experimental evidence of their activity should have been obtained within 6 to 10 months. It would appear, from the extent of the regeneration which occurs centrally, that some of the fibers might reach the periphery. These experiments yield no such evidence.

Several of the explanations which have been advanced to account for the recurrence of vasoconstriction, following sympathetic denervation of the upper extremity, appear applicable in certain cases. The increased sensitivity of smooth muscle to epinephrine may be an important factor in the early return of symptoms when postganglionic fibers are destroyed. Relatively complete denervation might relieve symptoms temporarily but be followed by their reappearance due to more effective activity of the persisting axons. Postganglionic fibers may be capable of functional regeneration. Our work indicates that recurrent symptoms, following the common operative procedures, may be due largely to the regeneration of preganglionic fibers from lower thoracic levels and their regaining synaptic relation with cells in the isolated upper thoracic ganglia.

SUMMARY

1. Following extirpation of the cervicothoracic and the second and third thoracic ganglia, regenerating unmyelinated and myelinated axons ascend from the cut end of the thoracic sympathetic trunk. The majority of these myelinated axons are preganglionic fibers which join similar fibers from the upper thoracic segments and reestablish functional connections with cervical sympathetic ganglia.

2. Evidence of reestablishment of functional connections by the preganglionic fibers was found, in most cases, after a postoperative period of four months.

3. A considerable number of unmyelinated fibers from the cut thoracic trunk reenter upper thoracic and lower cervical spinal nerves via the cut ends of communicating rami.

4. Physiologic tests failed to reveal functional activity of postganglionic fibers within a postoperative period of 300 days.

5. Capping the cut end of the thoracic sympathetic trunk in a glass or silver tube was only partially effective in preventing regeneration of axons from the severed trunk.

The authors wish to express their appreciation for the kind cooperation and interest of Dr. Harold Cummins, Professor of Microscopic Anatomy, Tulane University School of Medicine, New Orleans, La.

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TOTAL PANCREATECTOMY FOR HYPERINSULINISM DUE TO AN ISLET-CELL ADENOMA

SURVIVAL AND CURE AT SIXTEEN MONTHS AFTER OPERATION
PRESENTATION OF METABOLIC STUDIES

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WE WISH TO REPORT A CASE in which complete pancreatectomy was performed for hyperinsulinism due to a small islet-cell adenoma located in the head of the pancreas near the duodenum. The case has several interesting features justifying its report. It is probably the second or third total pancreatectomy, and the first reported case known to us of complete pancreatectomy with survival following operation for more than a few weeks. It is the first total pancreatectomy for a benign lesion of the pancreas. The adenoma discovered in the removed pancreas is one of the smallest functioning islet-cell tumors reported, if not the smallest. Most important is the fact that the patient is living and well at the time that this paper is written, 16 months after the operation. Observations on the resulting diabetes and digestive disturbances are recorded.

CASE REPORT

The patient, a Jewish woman, age 49, registered at the Mayo Clinic July 6, 1942. She complained of fainting spells which had occurred intermittently during the previous three years. There were several different types of attacks, consisting of unconsciousness, dizziness, blank spells and sweating spells, all of which had been relieved by the administration of carbohydrate varying from orange juice to intravenously injected glucose. During one of the patient's unconscious spells, her physician had obtained a concentration of sugar that was less than 30 mg. per 100 cc. of blood. There had been five severe attacks of unconsciousness lasting from one to five hours. The minor attacks were more frequent than those of more severe character, and varied from dizzy or blank spells to attacks of sweating. These lasted from five minutes to one hour. During the blank spells the patient would feel rather foolish and be somewhat confused. Sweating spells would occur almost every day between 10 A.M. and 12 M. They were characterized by drenching perspiration, weakness and slight confusion followed by nausea.

* Since this article was written, Doctor Priestley has been commissioned Lieut. Colonel in the Army of the United States.

They were relieved by orange juice or candy. The patient complained of feeling nervous and depressed, experiencing panicky sensations and feeling disoriented.

General physical examination showed the patient's weight to be 142 pounds (64.4 Kg.). The systolic blood pressure was 140 Mm. of mercury and the diastolic was 80. The results of examination of the heart, lungs and abdomen were essentially negative. Urinalysis, blood counts and serologic tests for syphilis gave negative or normal results. Roentgenograms of the head, thorax and lumbar portion of the spinal column were negative. The hepatic function, as shown by the bromsulfalein test, was normal. An electrocardiogram showed: Rate 93, sinus tachycardia, slurred Q.R.S. complexes in derivations I and III, notched Q.R.S. complexes in derivation II, left axis deviation, notched P waves in derivations II and III, low amplitude T waves in derivation III. Leads IV-R and CR-2 showed positive T waves. The fasting concentration of sugar was 42 mg. per 100 cc. of blood; the concentration of calcium was 9.4 mg. per 100 cc. of serum. A routine 36-hour fast was started, but at 12 hours the concentration of sugar was 52 mg. per 100 cc. of blood, and at 18 hours the patient had a severe hypoglycemic crisis starting with drowsiness and sweating, and merging into stupor and unresponsiveness, and then into complete loss of consciousness, lasting between one and one and a half hours. Her concentration of sugar taken after the onset of this crisis was 29 mg. per 100 cc. of blood. Recovery was slow after intravenous administration of 20 Gm. of glucose, followed by oral administration of 200 cc. of orange juice. Anorexia with severe headache and fatigue followed the crisis but complete recovery was reached in 30 minutes. The concentration of sugar rose to 108 mg. per 100 cc. of blood after the glucose and orange juice had been administered.

A diagnosis of hypoglycemia, probably caused by hyperinsulinism, was made. It was our opinion that a tumor of the islets of Langerhans was present.

Operation.—July 15, 1942: When the abdomen was opened, all of the visible structures, including the liver, appeared normal. There was no evidence of a malignant lesion. The pancreas was exposed by dividing the gastrocolic omentum along the greater curvature of the stomach and reflecting the stomach anteriorly and upward. Prolonged and careful palpation of the pancreas from the tail to the head did not reveal any evidence of tumor. The posterior aspect of the head of the pancreas was exposed by reflecting the duodenum medially but no lesion could be found in this portion of the pancreas. It was felt that there must be an adenoma present which was of the same consistency as the remainder of the pancreas and not situated on the surface of the gland, and that for this reason it could not be detected. At this time the situation was reviewed in consultation with Doctor Wilder, of the Metabolic Service, who was present at the operation, with the hope of determining the best procedure for the patient. It was known that she was incapacitated by her symptoms and it appeared quite certain that these symptoms were caused by hyperinsulinism. If only a portion of the pancreas were removed, it was known from experience that she would not be relieved unless an offending adenoma were present in the resected portion. Accordingly, it was decided to remove the entire pancreas.

The duct of Santorini was isolated approximately 1 cm. proximal to the duodenum and was ligated. The duct of Wirsung entered the common duct about 0.5 cm. proximal to the papilla of Vater, and this duct was ligated. The common duct was severed and ligated proximal to its entrance into the pancreas. The gastroduodenal artery, likewise, was severed and ligated. The head of the pancreas then was dissected free from the duodenum and mobilization of the gland toward the left was continued. Care was observed in order to avoid injury of the superior mesenteric vessels immediately posterior to the pancreas near the head of the gland, and the splenic vessels coursing along the superior border of the body and tail of the pancreas were preserved also. The pancreas then was removed in its entirety. The blood supply of the duodenum was then, of course, inadequate, and, accordingly, partial gastrectomy was performed, approximately

a third of the stomach and the first and second portions of the duodenum being removed and an anterior Pólya-type of anastomosis being made. The duodenal stump at about the level of the superior mesenteric vessels was inverted. The gallbladder then was joined to the posterior wall of the stomach to establish adequate internal biliary drainage by cholecystogastrostomy. The patient was given a transfusion of 1,500 cc. of blood during the operation.

Pathologic Report: The pancreas weighed 80 Gm. Following prolonged search and many transverse incisions into the pancreas, a cellular adenoma of the islands of Langerhans, measuring 8 x 5 x 5 Mm., was found situated in the head of the pancreas. The portions of the stomach and duodenum removed during the course of the operation were normal in appearance.

Postoperative Course.—The postoperative course was uneventful. The patient's weight on admission was 142 pounds (64.4 Kg.). On August 9, the first time after operation that she was weighed, her weight was 132 pounds (59.9 Kg.). This gradually fell and reach 128.5 pounds (58.3 Kg.) at the time of dismissal. The stools varied from two to six a day, usually about two to three after the patient began to take food. They were rather large, light colored and foul in odor at first, with some improvement by the time of dismissal. On August 4, the concentration of hemoglobin was 10.6 Gm. per 100 cc. of blood; erythrocytes 3,370,000, and leukocytes 5,600 in each cubic millimeter of blood. On August 19, the concentration of cholesterol was 216 mg. per 100 cc. of plasma, of cholesterol esters 121, of lecithin 301, of fatty acids 397, and of total lipoids 613. The concentration of calcium was 9.2 mg. per 100 cc. of serum. On August 1, after an Ewald test meal, the total acidity was 60 and the free hydrochloric acid 40; 150 cc. was recovered in an hour and this contained a moderate amount of fine food remnants.

Comment.—Reports of total pancreatectomy for benign or malignant disease of the pancreas are exceedingly rare in the literature. In 1908, Sauve[1] presented an extensive study on the subject of pancreatectomy involving the head of the gland. He collected data on 11 cases in which the operation was known to have been performed up to that time. He mentioned a case credited by Mayo-Robson at the Congrès de Paris, in 1900, to Billroth, in 1894, in which entire removal of the pancreas had been performed because of its involvement in a growth and the patient survived. Sauve was unable to find any published account of this case and he felt that there was insufficient evidence of the details to warrant its inclusion in his series. The only case listed in Sauve's series approaching total pancreatectomy was Franke's, in 1900. Here the surgeon attempted total removal because of the apparent involvement of the entire gland by a malignant lesion. He made the following statement: "Under the head of the pancreas, I found a little mass as large as a hazel nut, situated against the duodenum; I thought it was a question of a supernumerary pancreas, and I preserved it." The patient in this case had a good convalescence and showed only mild glycosuria between the fifth and nineteenth postoperative days and no further glycosuria till her death from recurrence of the carcinoma five and a half months later.

The fact that the patient enjoyed "perfect health" without evidence of diabetes until the recurrence of the carcinoma would seem to indicate from numerous reports on partial pancreatectomy on human patients that at least 10 per cent of the gland must have remained, regardless of whether or not

the small mass of tissue represented a supernumerary gland or an unresected portion of the head.

Recently, Rockey[2] reported a case in which he performed total pancreatectomy for carcinoma of the pancreas, with widespread involvement of the gland. His patient survived for 15 days. Necropsy revealed less than 1 Gm. of pancreatic tissue unresected.

Unless we have overlooked any cases, ours is the second authenticated case of total pancreatectomy for any cause ever reported, and the only case in which there was survival beyond the immediate postoperative period.

In March, 1942, Duff[3] presented an extensive *Arbeit* on the "Pathology of Islet-cell Tumors of the Pancreas." From his review of the literature he was able to make the following statement: "The hypoglycemia syndrome has not been observed in association with islet-cell adenomata of a diameter less than 1 cm." The measurements of the adenoma in our case were 8 x 5 x 5 Mm. Smaller adenomas have been reported but they have been found incidentally at necropsy and were not associated with clinical hypoglycemia.

Total pancreatectomy in this case appeared to be justified by the following consideration: Careful examination of the gland at operation did not disclose an adenoma. It was then obvious that the hyperinsulinism was due either to an undiscovered adenoma or to hyperfunctioning of islet cells. Partial pancreatectomy would cure the patient if the resected portion contained an adenoma and might cure the patient if hyperfunctioning islets were the cause of the patient's symptoms, as in the case reported by Graham and Hartman.[4] However, it has been our experience that partial pancreatectomy in cases in which islet-cell adenomas were not found has been disappointing and has required in some cases repeated resections without favorable results.

Total pancreatectomy, on the other hand, should remove the cause of hyperinsulinism, whether it is due to an adenoma or to hyperfunctioning islet cells, and should not be followed by important disturbance of digestion and nutrition resulting from loss of external pancreatic secretion, as has been shown by the work of Whipple and Bauman[5] in removing the head of the gland for carcinoma. The decision to remove the entire pancreas and to substitute for the incapacitating illness of hypoglycemia diabetes and external pancreatic insufficiency, which we felt could be controlled fairly well medically, has been a happy one—an adenoma which would have been left behind if partial pancreatectomy had been performed was removed and the patient was cured of hyperinsulinism.

THE EFFECTS OF TOTAL LOSS OF INTERNAL SECRETION OF THE PANCREAS

The metabolic problem resulting from complete pancreatectomy resolves itself into two main considerations: First, a deficiency of the internal secretions of the gland; and, second, a deficiency of the external pancreatic secretions. It has been shown, both experimentally in animals and in cases of partial pancreatectomy performed upon human patients, that more than 80 to 90 per cent of the gland must be resected before diabetes mellitus is

produced. In 1934, Graham and Hartman reported a case in which they resected 80 to 90 per cent of the gland for hyperinsulinism. The patient was one year old. No adenoma could be found in the resected portion of the pancreas. Complete recovery was attained, and the fasting concentration of sugar nine months after operation was 83 mg. per 100 cc. of blood. Other cases, in which the patients were adults, are reported in the literature in which as much as three-fourths of the gland has been resected and there appears to have been sufficient internal secretory function retained to prevent the occurrence of diabetes.[5] It was anticipated, of course, in our case that complete pancreatectomy would produce diabetes mellitus but we felt that this could be controlled adequately by diet and insulin. The mild degree of the resulting diabetes was not anticipated.

Our findings in regard to the degree of internal pancreatic insufficiency

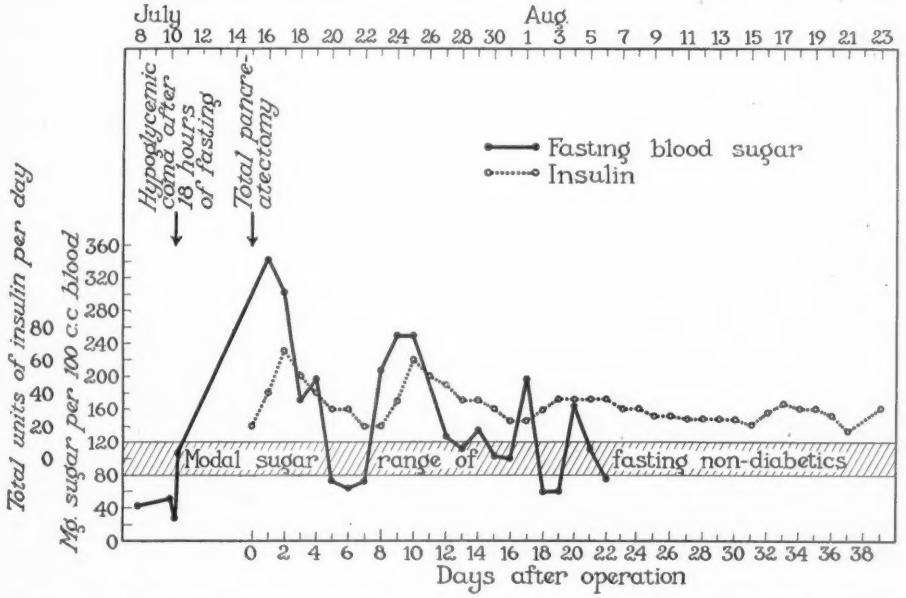
July
Aug.
8 10 12 14 16 18 20 22 24 26 28 30 1 3 5 7 9 11 13 15 17 19 21 23
Hypoglycemic coma after 18 hours of fasting
Total pancreatectomy
Fasting blood sugar
Insulin
Total units of insulin per day
Mg. sugar per 100 c.c. blood
360 320 280 240 200 160 120 80 40 0
80 60 40 20 0
Modal sugar range of fasting non-diabetics
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38
Days after operation

CHART 1.—Fasting concentrations of blood sugar and insulin requirements before and after total pancreatectomy.

are in close accord with those of Rockey in his recent report of total pancreatectomy for carcinoma. During the 15 days of postoperative survival of his patient's insulin requirement leveled off at a range of less than 27 units per day.

An interesting point was made in a recent article by Dragstedt[6] that it is necessary to remove 90 to 95 per cent of the pancreas of a dog to produce diabetes. The resulting diabetes, however, is very severe and, paradoxically, is more severe than if the total gland were removed. There are no published data known to us on man to make a similar comparison. However, in one case (unpublished) at the Mayo Clinic partial pancreatectomy was performed repeatedly for persistent hypoglycemia, and after the final

operation, which left only a small rim of pancreas adjacent to the duodenum, diabetes resulted which required between 60 and 100 units of insulin daily to control nearly one and a half years after operation. When this high insulin requirement is compared with the relatively small amount required to maintain control in Rockey's and in our case, after total pancreatectomy, the same paradox is noted as occurs in dogs.

As shown in Chart I, the fasting daily blood sugar reached a maximal height of 341 mg. per 100 cc. of blood on the morning after operation. The greatest total units of insulin required in any one day were 66. Regular, unmodified insulin was used for about four days after operation to "cover" the intravenous injections of 5 per cent solution of glucose in saline or distilled water. From about the fifth postoperative day the diabetes was controlled by single daily subcutaneous injections of protamine zinc insulin and regular insulin in a single combined dose, administered 20 minutes before breakfast. As will be noted in Chart I, the total daily dose that was required averaged around 30 units a day. The ratio of the two types of insulin varied from one unit of protamine zinc insulin to one to two units of regular insulin. The daily determinations of blood sugar were discontinued on the twenty-second post-operative day and the diabetes was controlled from this point on by testing the urine. Specimens of urine were obtained at 6 and 11 A.M. and at 4 and 9 P.M. The specimens of urine tested were fresh specimens, that is to say, the bladder was emptied by voiding a half hour before each specimen was obtained for testing. By the time of dismissal from the hospital the patient had been taught a system of adjusting her own combined dose of insulin so that the specimens of urine taken before breakfast and before supper showed a trace of sugar. Thus, the occurrence of insulin reactions was avoided but the diabetes was kept in adequate control.

At the time that the patient was dismissed the results of analysis of stools and urine were not available; therefore, the patient was sent home on the diet of 1,965 calories, basal plus 50 per cent, composed of 243 Gm. of carbohydrate, 94 Gm. of protein, and 70 Gm. of fat. No pancreatin was given. Adequate vitamin supplements were added. A letter received from her physician December 14, 1942, four months after her dismissal, stated that the patient was using "anywhere from 10 units of protamine zinc insulin and 10 units of regular insulin to 15 units of each every morning. She controls her dosage very well by checking her own urine. The urine is usually sugar-free. One month ago her fasting blood sugar was 109 mg. per 100 cc. Two days ago her fasting blood sugar was 177 mg. per 100 cc., this being after some holiday dietary indiscretion." Another letter stated that the patient "is doing very well. Her fasting blood sugar, taken two weeks ago, was 134 mg. per 100 cc. She uses just about the same amount of insulin. Her only complaint is severe abdominal cramps each morning." On July 16, 1943, her husband wrote that he was happy to say that "she is doing fine, has gained about three pounds (1.4 Kg.), eats practically everything, and is in fine spirits. She is really enjoying life. She also does

not weigh her food. She still has cramps for two to three hours every morning, but they are not as severe as at first." The latest report we received was in November, 1943. The dose of insulin still varied between 20 to 30 units per day.

As it has been established experimentally that fatty metamorphosis of the liver and hypolipemia usually develop, ultimately, in dogs adequately maintained with insulin unless they are given adequate amounts of raw pancreas, lecithin, choline or the extract of the pancreas or lipocaic,[6] a diet rich in choline was given to our patient to prevent the development of a fatty liver and hypolipemia. Fifty grams of cottage cheese was a daily constituent of the diet and this, together with a high protein content, was considered adequate to prevent such changes. The excellent health of the patient 16 months after total pancreatectomy is indirect evidence that such developments have not taken place. It has not been possible to obtain studies of function of the liver since dismissal.

EFFECT OF TOTAL LOSS OF EXTERNAL PANCREATIC SECRETION ON DIGESTION AND ABSORPTION

On the twelfth postoperative day the patient was taking a rather liberal solid diet, and the diabetes was under control. At this time, studies were begun to determine the degree of utilization of carbohydrate, protein and fat, and were carried out during two ten-day periods and one five-day period. It is possible that data obtained at a longer interval after operation would reflect the ultimate effect of total pancreatectomy better than those obtained so soon after operation. It is felt, however, that the data obtained are sufficiently interesting to warrant recording them.

The patient's basal caloric utilization was 1,310 calories, as computed by the Boothby nomogram. The three periods were kept essentially isocaloric at basal plus 50 per cent. This equaled approximately 2,000 calories a day. The cooked food was weighed and the content of carbohydrate, protein and fat was estimated according to Sherman's tables. In the first ten-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 241, 94.5 and 69 Gm.; in the second ten-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 206, 67.7 and 102.5 Gm. In the third five-day period the estimated daily intake of carbohydrate, protein and fat was, respectively, 222, 70 and 95 Gm. In the second and third periods the intake of protein was decreased approximately 25 per cent below the intake in the first period, while the intake of fat was increased 25 to 30 Gm. over it. The intake of carbohydrate, protein and fat was essentially the same in the third as in the second period. During the third period the patient was given 4.5 ounces (140 Gm.) of powdered pancreatin (Parke-Davis) in gelatin capsules (0.9 ounce [28 Gm.] a day). Data obtained during the third period, which was terminated at the end of five days because of the patient's objection to pancreatin, are not as statistically significant because of shorter duration of the period as those obtained in the

TABLE I

AVERAGE DAILY VALUES FOR FECAL SOLIDS AND CALORIES INGESTED AND LOST

	Calories											Fecal Solids					
	Intake				Loss												
Period	Carbohydrate	Protein	Fat	Total	Fecal Fat	Fecal Nitrogen	Urinary Sugar	Total	Balance	Basal Requirements	% Lost Feces and Urine	Total, Gm.	Fat, Gm.	% Total as Fat	Fecal N. as Protein, Gm.	% Total as Protein	% Total as Fat and Protein
I—10 days	962	378	621	1,961	433.71	207.00	32.64	673.35	1,287.7	1,310	34	131.97	48.19	37	51.75	39	76
II—10 days	825	271	923	2,019	326.52	101.64	10.88	439.04	1,580	1,310	22	83.94	36.28	43	25.41	30	73
III— 5 days	889	280	855	2,024	358.20	73.00	3.36	434.56	1,589	1,310	21	73.4	39.8	54	18.25	25	79

TABLE II

AVERAGE DAILY VALUES FOR INTAKE AND LOSS OF NITROGEN AND FAT

	Nitrogen									Fat								
	Loss, Gm.			Intake, Gm.			Balance,	% Intake Loss in		Loss in Feces, Gm.			Intake,	Balance,	% Fecal Fat as		% Intake Loss as	
Period	Urine	Feces	Total	Food	Pancreatin	Total	Gm.	Urine	Feces	Neutral	Split	Total	Gm.	Gm.	Neutral	Fatty Acid	Neutral	Fatty Acid	Total
I—10 days	5.27	8.28	13.55	15.12	0	15.12	+1.57	35	55	33.09	15.10	48.19	69	20.81	69	31	48	22	70
II—10 days	5.88	4.07	9.95	10.83	0	10.83	+0.88	54	38	19.40	16.88	36.28	102.5	66.22	54	46	19	16	35
III— 5 days	5.50	2.92	8.42	11.20	0.66	11.86	+3.44	46	25	22.40	17.40	39.80	95	55.20	56	44	24	18	42

first and second periods. A daily weight was obtained during the last 13 days of the study. This fluctuated within a range of three pounds (1.4 Kg.). The daily average number of stools varied but little from period to period, being 2.4 on the low fat and 2.8 on the high fat diet with pancreatin.

Methods.—The periods were begun and terminated by the use of carmine dye marker technic and feces and urine were collected for five-day periods. The stools were analyzed for total and neutral fat, nitrogen and carbohydrate, the urine for nitrogen and sugar. The total fat was estimated by the method of Saxon,[7] neutral fat by the method of Saxon, nitrogen was estimated by the method of Kjeldahl, and carbohydrate by the method of Folin and Wu. The results are given in Tables I and II.

Fecal Solids.—The average daily values for fecal solids are shown in Table I. The average daily weight of dried feces was greatest during Period I, when the loss of fat and nitrogen was greatest. The dried weight of the feces was greater than that of normal subjects on the standard Schmidt test diet, as reported by Pratt.[8] He found that the average daily weight of the dried feces of a series of six normal persons over a period of three days was 54 Gm. and that the maximum was 62 Gm. The average daily values obtained in Period I were comparable to those obtained by Pratt (113 to 154 Gm. a day for a three-day period) in five cases of carcinoma of the pancreas with obstruction to the pancreatic ducts, while the values in Periods II and III were increased only moderately above those in healthy persons.

The fat composed 37 to 54 per cent of the fecal solids (range in normal persons 8.5 to 28.5 per cent; average 18.5 per cent); 54 to 69 per cent of the fecal fat was neutral fat. The daily loss of nitrogen in the stools varied from 2.92 to 8.28 Gm. Computing the fecal nitrogen in terms of protein, average daily fecal protein accounted for from 25 to 39 per cent of the fecal solids. Fat and protein accounted for 73 to 79 per cent of the fecal solids.

Reducing Substances in the Feces and Urine.—Reducing substances in the feces were not measurable in Periods I, II or III. The average daily values for reducing substances in the urine are shown in Table I in terms of calories. These average daily values varied from 0.84 Gm. (3.36 calories) to 8.16 Gm. (32.64 calories).

Nitrogen Balance.—The nitrogen intake and loss are shown in Table II. The greatest nitrogen loss was observed during the period of greatest nitrogen intake (Period I). The nitrogen loss was less during Period III than during Period II, although the intake of both protein and fat was essentially the same during the two periods. Pancreatin was given during Period III and the smaller daily loss of nitrogen during this period appears to have been due to the pancreatin, in spite of the administration of pancreatin in gelatin, not enteric coated, capsules. The effect of this amount of pancreatin in gelatin capsules on the digestion of protein in this case accords with that of one of us (unpublished data of Comfort), and of Beazell, Schmidt and Ivy,[9] and Rekers, Pack and Rhoads,[10] on the effects of large amounts of

pancreatin given in enteric coated capsules in cases of external pancreatic insufficiency. The daily loss of nitrogen in the urine did not vary greatly in the three periods. The nitrogen balance was positive in Periods I and II despite a small loss of weight, but was more positive in Period I, in which the intake of nitrogen was greater than in Period II. The nitrogen balance was greater in Period III than in Period I, in spite of the greater intake of nitrogen in Period I. This may be due to the smaller daily loss of nitrogen in the stool and greater daily digestion and absorption presumably due to pancreatin.

Fat Values.—The average daily intakes of fat and the total fat in the stool during the three periods are shown in Table II. The proportions of ingested fat that was lost in the stool were, respectively, 70, 35 and 42 per cent in Periods I, II and III. The average daily value for total fat lost was greater on the low fat (69 Gm.) diet than on the high fat (102.5 Gm.) diet. The average daily value for total fecal fat was approximately the same in Period III, when the patient ingested a daily average of 95 Gm. of fat plus powdered pancreatin in gelatin capsules, as in Period II. In short, pancreatin administered in this fashion did not affect the absorption and digestion of fat significantly, contrary to the unpublished data of one of us (Comfort) and published data of Beazell, Schmidt and Ivy and of Rekers, Pack and Rhoads, on the effect of large amounts of pancreatin in enteric coated capsules in cases of external pancreatic insufficiency. The variations of the amount of neutral fat lost in the feces paralleled those of total fat. The percentage of total fat as neutral fat was greatest in Period I (low fat period) while the percentages of total fat as neutral fat were approximately equal in Periods II and III with an equal fat intake, in spite of the administration of pancreatin in Period III. Pancreatin, as given, did not affect the digestion of fat significantly in this case.

The Effect of Loss of Food in the Urine and Feces on Caloric Balance.—The caloric values of the ingested food and of the foods recovered in the urine and feces are given in Table I. The average daily caloric values of the foods ingested varied but little in the three diets. The loss of food in the urine was small; that in the feces was heavy. Metabolic fecal fat and nitrogen have been ignored in computing the balance. The average daily loss of calories was 673, 439 and 435, respectively, during Periods I, II and III, and 34, 22 and 21 per cent of the caloric intake was lost during these same periods. The calories utilized were approximately equal in number to those for basal requirements during Period I and were only slightly in excess of basal requirements in the other two periods. The caloric loss was found to be great enough to affect the estimated necessary caloric intake radically.

SUMMARY AND CONCLUSIONS

A case of hypoglycemia due to hyperinsulinism from a small adenoma of the islets of Langerhans in which a total one-stage pancreatectomy was performed is reported herewith. A less radical procedure would have failed to

cure the patient, since the adenoma was located in the head of the gland, in intimate proximity to the duodenum. We believe that this is the first case of total pancreatectomy for benign or malignant disease in which the patient has survived beyond the immediate postoperative period. Total pancreatectomy was followed by a relatively mild degree of diabetes. Disturbance of carbohydrate digestion was not detected by the methods used, while digestion of protein and fat was definitely diminished. About 35 to 70 per cent of ingested fat and 25 to 55 per cent of ingested nitrogen could be accounted for in the feces. A positive nitrogen balance occurred in spite of the large loss of nitrogen in the feces. Foodstuffs in the urine and feces accounted for 21 to 34 per cent of the calories ingested. The percentage of total fat in the stools as neutral fat varied from 54 to 69 per cent. The dried weight of the stools was greater than values obtained for healthy persons. The patient has remained in excellent health, 16 months after the operation. Evidence of deficiency of lipocaic has not developed.

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TOTAL GASTRECTOMY, SPLENECTOMY, RESECTION OF THE LEFT LOBE OF THE LIVER, OMENTUMECTOMY AND COLECTOMY UPON ONE PATIENT IN ONE OPERATION

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A REPORT of the removal of the stomach, with resection of the left lobe of the liver, the spleen, omentum and entire colon at one operation, may seem only prideful, in view of the fact that the patient died after the second-stage closure of the Mikulicz anastomosis of the lower sigmoid and terminal ileum, five months after the original operation. However, a report of the case serves to illustrate modern progress in anesthesia and surgery and to demonstrate the amount of surgery a patient, even of advanced years, in this surgical era can survive.

REPORT OF CASE

A male, age 66, was referred to the Lahey Clinic with a history suggesting carcinoma of the stomach, and a roentgenogram showing evidences of a tumor occupying a large

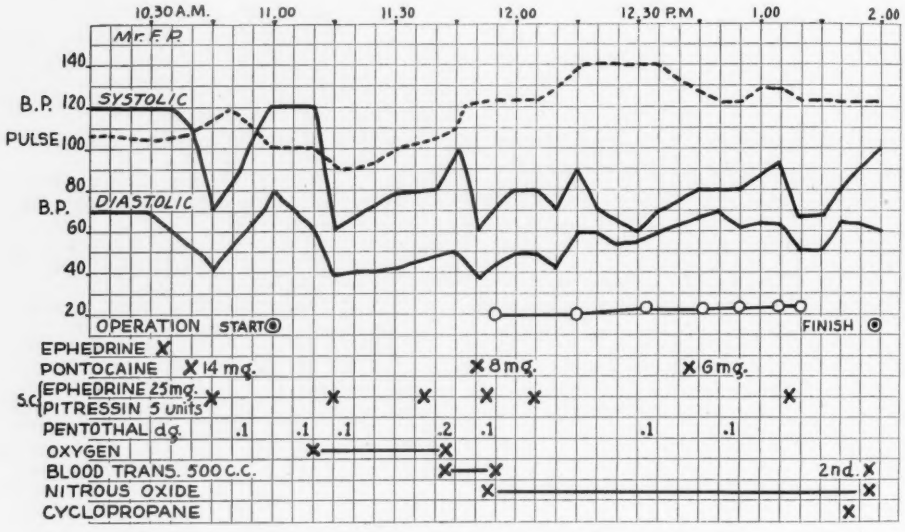

CHART 1.—Showing the data recorded during the prolonged, continuous fractional anesthesia.

part of the stomach. The diagnosis was probable carcinoma of the stomach, and he was submitted to surgery, with a prospect of total gastrectomy.

The operation was performed under fractional spinal anesthesia. The anesthesia record showing the time consumed, pulse and blood pressure is shown in Chart 1.

Upon opening the abdomen, the median portion of the stomach was found to be occupied by a large firm mass assumed to be a carcinoma (Fig. 1). Included in this mass by contact invasion was the left lobe of the liver. Likewise included in the mass

by contact extension was the midtransverse colon up to the splenic flexure. As the transverse colon was turned up to inspect the jejunal fossa, this extension to the transverse colon was found to reach into the mesentery of the transverse colon next to the bowel and to involve the middle colic artery. There was a considerable area of mesenteric root that was uninvolved.

While on first inspection the mass seemed hopelessly irremovable, further investigation revealed no nodes in the gastrocolic or gastrohepatic omentum, and no metastases in the liver except where the gastric mass had involved the left lobe of the liver by contact extension. The mass, which was freely movable and sharply demarcated, was

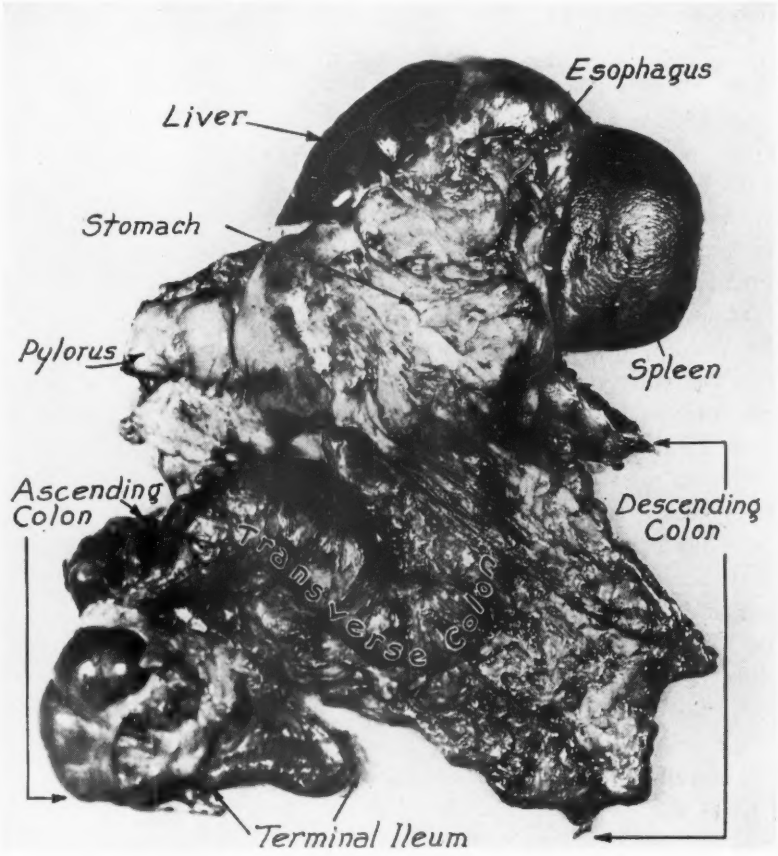

FIG. 1.—Photograph of the gross specimen of the composite mass of viscera removed.

evidently of an unusual nature. Although apparently malignant, occupying a large portion of the stomach, it had not extended into the lymph nodes, and if one cared to accept the hazards of such an extensive procedure, it was removable. Although the patient was 66 years of age, he was thin and wiry, and preoperative study had revealed nothing abnormal except the gastric lesion. It was, therefore, decided to accept the risk.

Because the transverse colon with its middle colic artery was involved, it seemed best to transect the ileum, tie the blood supply and free the entire colon (ascending, transverse and descending) from the ileum down to the sigmoid, sewing the ileum to the sigmoid to make a Mikulicz anastomosis. The liver was cut across where the left lobe joins the right lobe, controlling bleeding with the fingers until mattress sutures of silk

could be inserted. The spleen was freed and turned up, its vessels were tied at the tail of the pancreas, and the whole block of organs, the left lobe of the liver, stomach, omentum, spleen and entire colon, was then removed in one mass. The duodenum was inverted and closed and the jejunum anastomosed to the esophagus as in any total gastrectomy.

In the interval between the original operation and the secondary closure of the Mikulicz anastomosis, the patient was driven by motor 250 miles to his summer home in the mountains. His weight was maintained but did not increase. Three months after operation the Mikulicz opening was successfully closed, but the patient died two months later due to what was proved by autopsy to be a recurrence of the malignant lesion. The pathologic report was Hodgkin's disease of the stomach.

COMMENT

On review of the case, the operative undertaking was not as reckless as it may appear to the reader. At the Clinic many total colectomies for ulcerative colitis and polyposis have been performed successfully. Splenectomy, likewise, has been undertaken in many total gastrectomies and adds but little to the time and the technical steps of the procedure. Resection of the left lobe of the liver is not a difficult technical undertaking since its ligamentous attachment to the diaphragm is avascular, easily detached and permits such mobilization of the left lobe that it readily can be severed from the right lobe and the bleeding accurately controlled by mattress sutures.

With the entire colon and omentum removed, together with the spleen, stomach and left hepatic lobe, the remaining abdominal contents, largely right lobe of the liver and small intestine, only partly filled the abdominal cavity and so made exposure and suture of the jejunum to the esophagus extremely easy. In fact, in none of the 73 total gastrectomies which have now been performed at the Clinic has the exposure been as complete, and the anastomosis as easy, as in this case after removal of all the organs that so often interfere with exposure.

The Mikulicz plan of anastomosis of the ileum to the sigmoid, the usual procedure in colon resections in this Clinic, lessened the time required for the anastomosis, eliminated any additional hazard of leakage, and permitted immediate decompression of the small intestine through the tube inserted into the ileac end of the Mikulicz anastomosis.

Without the excellent continuous spinal anesthesia provided by the Department of Anesthesiology of the Clinic, I doubt that this extensive operation could have been accomplished successfully.

SUMMARY

The patient described had the most extensive operation ever undertaken in my experience, namely, total gastrectomy, splenectomy, omentumectomy, colectomy, and resection of the left lobe of the liver. The technical surgical details are given, together with a photograph of the specimen and the anesthesia record. Although the removal of this large amount of abdominal contents was not justified in view of the short period of survival of the patient, the successful technical accomplishment of the operation is proof of the modern advances in anesthesia and surgical methods.

AN EXPERIMENT IN THE EARLY DIAGNOSIS OF GASTRIC CARCINOMA*

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THE RECORD of the patients with carcinoma of the stomach at the Presbyterian Hospital, we believe, is not unusual. During the 35 years from 1908 to 1942, inclusive, 1204 people with carcinoma of the stomach were admitted to the hospital. Of this number 231 underwent resection, of whom 64 died as a result of the operation, leaving 167 who were discharged after radical surgery. Even this number includes a few cases in which the surgeon knew he left tumor behind, or the pathologist demonstrated unsuspected tumor cells at the limit of the resection. We face the fact, then, that of all the people who came to the hospital during this period with this condition less than 15 per cent left it with any possibility that their disease had been arrested.

There are several obvious means by which this record could have been improved, which we have attempted in recent years to employ: (1) A more alert attitude on the part of the internists into whose hands the patients usually come first, so that early carcinomas are less often overlooked. (2) Better technic on the part of the radiologists and gastroscopists in demonstrating suspected lesions. (3) Willingness on the part of the surgeons to operate when, after careful study, some suspicion of carcinoma still exists. (4) Wider resections, and resections of tumors formerly considered inaccessible. In our clinic, as in many others throughout the country, this is being done. (5) A lower operative mortality rate. Our rate has dropped from 33.8 per cent for the period 1908 to 1937, to 17.9 per cent for the period 1938 to 1942, and to 4.7 per cent for the year 1942.

We believe that all these factors have played their part in raising our resectability rate from 14.8 per cent for the period 1908 to 1937, to 36.5 per cent for the past five years. Before 1938, less than one patient in ten with gastric carcinoma left the hospital with any possibility of arrest of his disease; now during the past five years the ratio approaches three in ten. Whether this apparent improvement will result in more five-year survivors, there has not yet been time to tell. It will follow, probably, that the rate of arrest will not keep pace with the resectability rate but rather with another

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factor, namely, the proportion of cases that come to surgery free of metastases. Our reason for this belief lies in the following statistics. Of the 97 patients who survived resection prior to April, 1938, 25 (25.8 per cent) lived five years, or more, apparently free of their disease. This is a most encouraging figure, which shows that radical surgery for carcinoma of the stomach under proper circumstances does offer hope of cure. But it is significant that of these 25 survivors only four were shown to have metastases at the time of operation. When one recalls that these four were the sole survivors of about 900 with presumable metastases who were admitted during this period, the importance of early diagnosis becomes obvious.

This does not mean that the measures which were taken to improve our results have been futile. Certain advances have been made. The number of admitted cases who were found to have no metastases prior to 1938 was about 6 per cent; during the past five years it has been nearly 10 per cent. Of importance, too, is the fact that a greater proportion of cases without metastases have survived resection. Perhaps, also, more cases with metastases will prove to have been saved by the wider resections now being undertaken. In other words, we are providing our surgeons with a more hopeful group of cases, and they are being better treated. But it is still true that the great majority of cases enter the hospital already hopelessly ill, and it is within this group that improvements must be made if the death rate from carcinoma of the stomach among the general population is to be significantly reduced.

TABLE I

CARCINOMA OF THE STOMACH
1908-1942 (Inclusive)

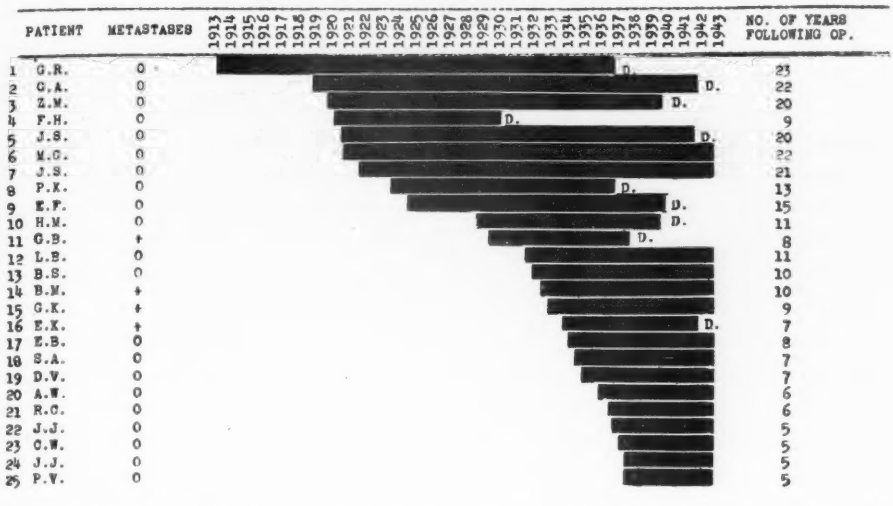
	1908–1937	1938–1942	Total
Admissions	960	244	1204
Operations not for cure	471	95	566
Resections	142	89	231
Resection rate	14.8%	36.5%	19.2%
Resection operative mortality	33.8%	17.9%	27.7%
Metastases absent	56	24	80
Metastases absent (survived resection)	41	21	62

It is this large group which comes to the doctor too late for attempts to cure that is the main subject of our study. They come too late usually because the early symptoms of gastric carcinoma escape their notice or do not seem to them important. To them may be added, unfortunately, the patients whose gastro-intestinal studies were delayed because the doctor whom they first consulted failed to elicit complaints or appreciate their significance. Clearly, if the surgeon waits for these people to come to him, they will continue to come too late. Therefore, he must reach out and bring them in to study before they are aware of trouble, if possible while their disease is yet asymptomatic. Much has been done for pulmonary tuberculosis by mass studies of people who did not suspect that they had the disease, and we have made an experimental attempt similarly to attack gastric carcinoma.

The attempt consisted of mass roentgenologic studies of men and women who were not suspected of having gastric lesions. The subjects of the study were people over the age of fifty who had no digestive symptoms of appreciated significance. It was impossible to limit the group precisely, because few people have no digestive symptoms whatever. In selecting our cases we tried to include only those people who ordinarily would not have received

CHART I

CARCINOMA OF THE STOMACH
FOLLOW-UP RESULTS AFTER PARTIAL GASTRECTOMY
LIVED 5 YEARS OR MORE WITHOUT EVIDENCE OF RECURRENCE



a gastro-intestinal study, so that if they had a gastric lesion it would not ordinarily have been discovered. Maintaining this prerequisite, we first studied patients from the Surgical Follow-up Clinic, who had been treated for conditions other than gastric. We endeavored subsequently to examine every person over the age of fifty who came to the hospital, whether as a patient or a relative or friend. It was not difficult to persuade most of these people to come for examination and they were usually happy and grateful to know the result. We saw little evidence of arousing undue fear of cancer. This part of the study really comes under the province of public health. Controlled groups such as members of large corporations or civic departments should be the easiest to handle.

The study is yet incomplete but the results are beginning to be of interest. Two thousand, four hundred and thirty-two persons have been examined, of whom 491 have been reexamined a year, or more, later, making a total of 2923 examinations. Nineteen cases have been deducted from this study because they were admitted to it in error, in that they had important gastric symptoms. This leaves a net of 2413 new cases that have been studied. Of these, three had proven unsuspected malignant gastric tumors, two of which were carcinomas and one of which was a lymphosarcoma. The inci-

dence of unsuspected malignant tumors found was, therefore, 1.24 per thousand. These three cases underwent subtotal gastric resection.

The method of study is essentially a rapid fluoroscopic examination of the stomach. It is based on the belief that an experienced roentgenologist rarely requires more than a minute to satisfy himself by gastric fluoroscopy that he is dealing with normal findings. No attempt was made during our rapid examinations to determine more than the one fact, namely, did the stomach show evidence of abnormality or did it not? If nothing abnormal was noted, the patient was dismissed. If any suggestion of abnormality was seen, the patient was brought back for further careful study at a later time. The examination was made in the erect position only, unless something suspicious was found in the fundus, in which case the patient was also examined prone. The first thousand cases received a single stomach film to check the rapid fluoroscopic examination, but, as nothing was found on any of the films that had not been noted at fluoroscopy, the films were thereafter omitted. Using the present routine, it is possible to examine as many as 40 patients an hour. The chief difficulty has been not the speed of the examination but the handling of the patients, guiding them back and forth from the dressing rooms, keeping them flowing steadily into the fluoroscopic room, *etc.* It has required two assistants and a stenographer to keep the examiner busy.

The objection has been raised to this method that, inasmuch as errors are frequently made at roentgenologic examinations of the stomach under the best circumstances, one might infer that so rapid an examination as we employ would lead to many more. It must be recalled, however, that at our rapid examination only one point is determined, namely, the presence or absence of an abnormality. Our experienced roentgenologists in their routine practice, over the years, have not required more time to make this determination, so that the rapid examination should in this respect be as accurate as the routine studies. Admittedly, the examination is as good as the roentgenologist, and no better. It must be done by someone with experience. One cannot expect perfection of the method. Only trial can tell how accurate it will prove to be, but even if it were only 50 per cent reliable it still might discover many early carcinomas that now go on to the inoperable stage. The study has not progressed far enough to prove or disprove the value of mass examinations of people in this manner. Unfortunately, the entire project is for the time being interrupted by war conditions. We are merely recording our findings thus far.

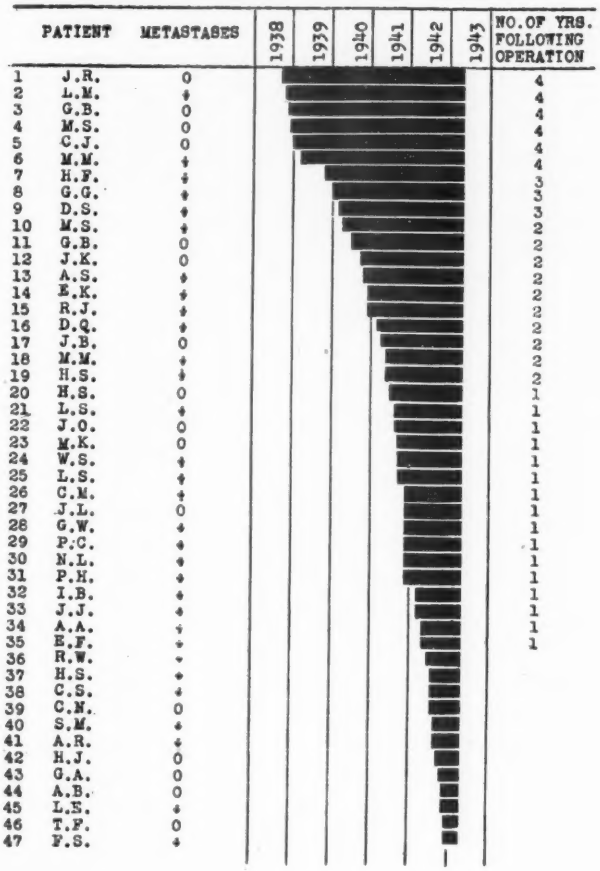
The most encouraging aspect lies in the three malignant lesions found and the nature of them. The first, a lymphosarcoma, was discovered at fluoroscopy because of a persistent area of flattening near the pylorus. This was confirmed by further roentgenologic studies, but at operation our senior surgeon was unable to appreciate any lesion even with the stomach opened and, therefore, did not resect. Some months later, at the site of the suspicious roentgenologic finding, an obvious tumor developed which was then resected and proved to be a lymphosarcoma. The patient later died of her disease. The note-

worthy fact in this case is the discovery by quick fluoroscopic study of a lesion so small that an experienced surgeon could not appreciate it at operation. The second case of malignant disease found was a double carcinoma of fungating type in the fundus of a 60-year-old man who came to the hospital

CHART II

CARCINOMA OF THE STOMACH
FOLLOW-UP RESULTS AFTER PARTIAL GASTRECTOMY
1938 - 1942 ALIVE WITHIN 5-YEAR PERIOD

	PATIENT	METASTASES	NO. OF YRS. FOLLOWING OPERATION
1	J.R.	0	4
2	L.M.	+	4
3	G.B.	0	4
4	M.S.	0	4
5	C.J.	0	4
6	M.M.	+	4
7	H.F.	+	3
8	G.G.	+	3
9	D.S.	+	3
10	M.S.	+	2
11	G.B.	0	2
12	J.K.	0	2
13	A.S.	+	2
14	E.K.	+	2
15	R.J.	+	2
16	D.Q.	+	2
17	J.B.	0	2
18	M.M.	+	2
19	H.S.	+	2
20	H.S.	0	1
21	L.S.	+	1
22	J.O.	0	1
23	M.K.	0	1
24	W.S.	+	1
25	L.S.	+	1
26	C.M.	+	1
27	J.L.	0	1
28	G.W.	+	1
29	P.C.	+	1
30	N.L.	+	1
31	P.H.	+	1
32	I.B.	+	1
33	J.J.	+	1
34	A.A.	+	1
35	E.F.	+	1
36	R.W.	+	
37	H.S.	+	
38	C.S.	+	
39	C.M.	0	
40	S.M.	+	
41	A.R.	+	
42	H.J.	0	
43	G.A.	0	
44	A.B.	0	
45	L.E.	+	
46	T.F.	0	
47	F.S.	+	



because of a urethral stricture. Slight gastric symptoms were present but had not attracted his attention. A subtotal gastric resection was performed. No evidence of metastases was found either at operation or at pathologic examination. The third malignant lesion occurred in a man, age 54, who came to the hospital because of a large hydrocele. This carcinoma was situated near the pylorus. It presented an ulcerated area less than one centimeter in diameter. The tumor had penetrated the muscularis mucosae and invaded the submucosa but had entered the muscularis only at one small area. It had not metastasized. This is one of the earliest gastric carcinomas ever found at the hospital.

The nature of these three tumors has been a source of great encouragement to us. Two were very small when discovered, showing that tumors of this size can be discovered by our method. The two carcinomas which were found had not metastasized, which places them in the group of relatively good prognosis. There is no reasonable doubt that these three patients would have come to operation far later if they had been allowed to progress to the symptomatic stage.

There were five other cases who underwent gastric resection because of suspicion of gastric carcinoma but in whom only benign single or multiple ulcers were found. They were subjected to extensive roentgenologic study, and most of them to conservative therapy and gastroscopy before operation. Some of them had symptoms before being brought in for their first rapid fluoroscopy, but none had any intention of consulting a doctor about them. We have felt for some time that it is safer to resect stomachs in people over age 50, with persistent gastric ulcerations than to wait perhaps for a carcinoma to become all too obvious. One of the five died of a postoperative pulmonary embolus. The other four are symptom-free. These cases illustrate the difficulty in making an exact diagnosis in gastric lesions, even with all the diagnostic aids available.

An additional 15 cases were brought back for careful study because the first rapid fluoroscopic examination suggested some abnormality that might be due to a new growth. Their lesions were all considered to be benign, and were not subjected to operative exploration.

An interesting by-product of the study has been the relatively large number of abnormalities other than carcinoma that have been discovered. These include conditions both functional and organic. Five hundred and twenty-eight such instances were noted. The greater percentage, of course, were functional derangements. However, there was a surprising number of organic derangements. For example, 54 instances of deformed duodenal bulb were found, without symptoms of ulcer. Some of these had actual craters, but the majority showed the deformity of previous ulcers only. These were in people who "had never had any trouble with their stomach." There were seven instances of cardiospasm and 25 cases of diaphragmatic hernia, two of which were rather large. An idea of the incidence of other irregularities was obtained, such as anomalies of position of the stomach and duodenum, diverticula of the stomach and duodenum, evidence of "gastritis," *etc.* One polypus of the stomach was found. Ninety abnormalities within the thorax were noted and occasionally gallstones, *etc.*

The cost of the examination has been approximately 48 cents a person. This does not include the cost of the roentgenologist's services or the overhead charges for the roentgenologic equipment, but the actual cost of secretarial and technical help, stationery, films, *etc.* One of the chief difficulties has been to get people for examination as fast as we wanted them. While the method is still in the experimental stage, we have not been able to interest life insurance companies or city institutions in helping us to obtain

larger numbers of people for study. We have been limited to the people who have come to our own institution, although we could have well handled many times this number.

The study should be continued for many years to prove its value. We are particularly interested in seeing what evidence we can discover of the accuracy of the method. It is as yet too early to say what proportion of new growths we may have missed. Among the 491 people that we examined a year or more after their first examination, no tumors were found. We are aware of one error which happened on a morning when a junior roentgenologist was making the examinations and somehow overlooked a very large and obvious growth. The case is not included in our series because the patient had severe symptoms, but we must, in honesty, make mention of it. Otherwise, so far as we know, we have missed no tumors.

Whether this method is a practical one for reducing the large number of incurable gastric carcinomas that come to our hospitals we cannot yet say. At least one thing should come of it, if nothing else, and that is an opportunity to learn more about the characteristics of early gastric carcinoma, for our experience so far has, unfortunately, been chiefly with its late manifestations.

THE FREQUENCY AND FUTURE OF GALLSTONES BELIEVED TO BE QUIESCENT OR SYMPTOMLESS*

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ALTHOUGH A NUMBER of objections to a general exploration of the peritoneal cavity as a routine part of an abdominal operation can be brought forward, an investigation of the region of the gallbladder, when permissible, is often more informative than is the invasion of the other quadrants.

The palpation of the gallbladder in an additional 150 cases during the course of abdominal operations performed upon women for conditions other than those relating to this structure, now makes possible a review of a series of 500 personal cases in which this procedure has been carried out.[1]

By direct palpation of the gallbladder through celiotomy incisions in 500 women, stones were found to be present in 50, or ten per cent of the cases so examined.

This investigation presented two attractive opportunities: First, to contribute something toward establishing what may be accepted as the percentage of occurrence of gallstones in women, and then to attempt to gather some authentic information as to so-called quiescent or symptomless gallstones.

To discover the presence of gallstones in as many as ten per cent of 500 women not supposed to possess them at the time of discovery would seem to call for comment at least, if not explanation. However, there is good reason to believe that the actual percentage of occurrence among these women may have been even higher. As the stones in each case were discovered by direct palpation, it is probable that there were very few, if any, instances of mistaken identity. On the other hand, it would be quite remarkable if there were no stones present that escaped detection among 500 gallbladders palpated; and for good reasons. It is common experience to find small stones present in a gallbladder when opened after removal that had not been detected during the course of the operation. In the great majority of cases included in this series the gallbladder was examined through a lower abdominal incision, this definitely limiting the facility of examination. Conditions of or about the gallbladder itself, such as adhesions; a large and tense gallbladder; a bladder wall thickened and more or less rigid from chronic inflammation; or one or more small stones floating about in a considerable amount of bile either in the fundus or deep down in the ampulla, at times favored failure to appreciate a stone or stones present.

Allowance must also be made for the fact that this investigation was

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carried out in women only, most of whom had had pregnancies, and most of whom were at an age when biliary disease is most commonly experienced.

Furthermore, there is no evidence to support an opinion that the various conditions bringing these patients to operation had had a share in the conditions resulting in the formation of the stones discovered.

When all the many factors involved have been brought forward and duly considered, and such allowances and adjustments made, as may be necessary, it is probable that the ten per cent incidence of occurrence of gallstones in this group of 500 women would be duplicated in another group similar in size, in nationalities and social status, in ages and in conditions of childbearing, and that in both it would closely approximate reality.

Merely to find stones in 50 women not supposed to possess them before discovery, does not, without additional information and study contribute materially to existing knowledge as to so-called quiescent or symptomless gallstones.

A tendency to concentrate too much upon the condition presenting itself for operation and to omit entirely other inquiries into the past history, sometimes resulted in failure to bring into the picture information that might have suggested the occurrence of biliary disease either as an episode of the past or as an existing complication.

When the histories of some cases were supplemented following the discovery of the stones, it was found that not infrequently there had been evidences of their presence which were made more or less apparent in one of three ways: There may have been symptoms so slight as to be considered of little or no significance and readily accounted for by indiscretions of diet, indigestion or other common causes. There may have been one or more suggestive or typical attacks in the more or less remote past neither voluntarily reported nor previously inquired into. Finally, it became clear that some patients were actually having gallbladder symptoms at the time, which were erroneously attributed to, or more or less obscured by, the surgical condition obviously present.

In a consideration of the potentialities of inactive gallstones, a useful distinction can be made between those that have asserted their presence on one or more occasions, but at intervals of considerable duration, and those that have never caused symptoms, so far as can be determined, applying the term quiescent to the former variety and symptomless to the latter. Among the 50 patients composing this group of cases there have been satisfactory examples of each type, many more of the first than the second.

It is disappointing that the sources of knowledge as to inactive gallstones are so few and that these are unsatisfactory, since, for the most part, they seem to withhold at the same time that they contribute much valuable information. Many such stones undoubtedly exist and escape detection altogether, while others, even though discovered, are of entirely known duration and still others are promptly removed, thus terminating a possible chance to observe future behavior.

The plain roentgenogram occasionally shows a stone or stones not previously suspected of being present. But it is not possible to demonstrate the presence of the great majority of gallstones in this way.

Not unnaturally, cholecystograms are rarely if ever resorted to in the absence of suspicions regarding the gallbladder, while as to the many instances of unsuspected gallstones found in the gallbladder at autopsy, the absence of reliably recorded gallbladder symptoms does not justify the assumption that there had not been such at any time prior to the demise of the individual found to possess them.

It is probable that there is no better opportunity available at the present time to establish instances of quiescent or symptomless gallstones than by the digital examination of the gallbladder through the abdominal incision. Thus found, it is often possible to combine a careful past history with the developments of the future in an endeavor to isolate cases that can be accepted as instances of one type or the other.

It would seem that the discovery of the presence of gallstones with the abdomen already opened might be followed by the removal of the gallbladder in a majority of the cases. There were several reasons why this policy was not adopted.

Biliary disease not having been suspected before operation, it had not been discussed with the patients and consent to operation upon the gallbladder had not been obtained should this be indicated.

The great majority of the incisions were made in the lower half of the abdomen and there was reluctance to resort to either an undesirable extension of the existing incision or to add a second incision.

In many cases the condition bringing the patient to operation was quite sufficient, in itself, without superimposing a second major operative procedure, with its additional risks.

Over and above all of these considerations was the feeling that the presence of gallstones requires more than the mere removal of the gallbladder. The initial operation upon the biliary system offers the most favorable opportunity to deal satisfactorily, and usually finally, with the individual type of the disease present, and demands a suitably located incision, an adequate exposure, a thorough search for, and examination of, such biliary pathology as may be present, as well as an inspection of adjacent and associated structures, and an unhurried and carefully performed operative procedure adapted to the particular requirements of the individual patient.

In the few cases where the gallbladder was immediately removed, there was either an error in diagnosis and the gallbladder being the sole offender and the only lesion present, or, combined with the pathology that had been the operative indication, it was suspected of being responsible for an important part of, or perhaps all of the patient's complaints.

The reactions of the various patients when informed as to the presence of their gallstones were variable, as might have been expected. Some welcomed the news as an explanation or confirmation of occurrences of

the past; some, having just experienced a generous dose of surgery, were considerably distressed; while still others were apparently incredulous or made light of their condition, having undoubtedly been quite free from impressive symptoms in the past, a circumstance that would assist in explaining the unexpected discovery of the stones.

Surprisingly few seemed to entertain the idea that there was need or reason to be relieved of their stones. Almost without exception the patients were informed at a suitable time as to the presence of the stones. In the absence of contraindications the removal of the gallbladder was not merely recommended but advocated. In surprisingly few cases was this advice accepted, only the onset of acute symptoms in most instances being persuasive, and even this often only after surprisingly long periods of delay. The reluctance to agree to operation was undoubtedly often due to the fact that the majority of the stones had produced few or no really urgent symptoms to emphasize the announcement of their presence, or there had been but a single and almost forgotten attack in the remote past.

The majority having declined operation upon their gallbladders after the facts had been placed before them, the desirability of establishing and continuing contact with each of these patients possessed of gallstones was quite obvious, and this was done, so far as possible, for variable periods up to 20 years or more.

These composed a most favorable group to look to for possible information as to quiescent or symptomless gallstones, and were followed with particular zeal for this reason rather than that many of them were expected to eventually come to cholecystectomy.

An effort was made to discover among the members of the group a few cases, at least, that might be termed symptomless gallstones and still others that might be regarded as quiescent. As was expected, a number of patients sooner or later did develop the necessary symptoms to bring them to operation, while, almost at once, two problems presented themselves as to some of the others. Knowing of the presence of the stones it became necessary at times to distinguish between minor digestive disturbances that would have been considered insignificant in other individuals and accounted for by the usual common causes, and identical complaints that had their origin in the gallbladder pathology itself.

Again, in a few cases, it was difficult, even sometimes impossible, to feel assured of the entire absence of symptoms that might be legitimately related to the gallbladder, even after the most careful, indirect and frequently repeated questionings.

It is at times no mean accomplishment to formulate an unambiguous question, to convey this to, and have it clearly comprehended by, the individual to whom it is directed and then to receive in return a precise and convincing answer.

This fact became particularly apparent when the necessity of obtaining

precise and essential information was found to depend almost exclusively upon the processes of interrogation.

Only six of the original 50 cases can be listed as having been both free from all symptoms since the appreciation of the stones and as having remained under observation up to the present time.

Two of these give a past history of doubtful accuracy, certainly, sufficiently so to disqualify them for listing as never having had symptoms.

One other had had quite definite symptoms in the past, and one might have had symptoms mixed with those of a gastric ulcer.

Two cases, having been under observation for periods of 9 and 15 years, were sufficiently clear-minded and responsive to give satisfactory assurance as to the entire absence of all gallbladder symptoms in their past histories, and having been equally free from all symptoms while under observation.

A number of instances of long periods of quiescence of gallstones were discovered among the 50 gallstone cases. Apparently, it is not uncommon for a single typical attack to occur and then be followed by such a long period of freedom from symptoms as to create the impression that it was the final one. This seems to be a phase of the natural history of gallstones that is not uncommon and is generally recognized.

In order to obtain additional information as to the condition of the gallbladders of some of the patients found to possess stones and perhaps confirm the findings of cholelithiasis, roentgenologic examinations were made in such cases remaining under observation as were willing to cooperate in this investigation and where conditions permitted. There were ten of these, eight having cholecystograms and two plain films.

In four of these cases it was found that the gallbladder did not fill with the dye and that the gallstones were not visualized. These cases had gone for 10, 14, 18 and 21 years, respectively, since the discovery of the stones, two of the four having had symptoms at some time or other during the period (Cases 1, 6, 17 and 18).

In three cases the dye entered and left the gallbladder, the stones being demonstrated in each case. One of these examinations was made two weeks after the discovery of the stones, the patient apparently having mild symptoms, another five years after the discovery of the stones, there having been no symptoms; and the third, 13½ years after the discovery of the stones, there never having been any symptoms (Cases 23, 34 and 47).

In one case the dye did not enter the gallbladder but the stone could be seen four years after its discovery, there having been mild, though definite, symptoms in recent months (Case 37).

In two cases the presence of the stones could be shown in the plain film, three and one-half and six years, respectively, after their detection, the former case having had no symptoms, the latter having had annoying and persistent digestive disturbances the greater part of the entire period (Cases 35 and 50).

The relation of typhoid fever to this group of cases, and especially to the cases found to have gallstones, was of considerable interest. Two hundred fifty-nine of the 500 patients were questioned as to typhoid fever and 13, or five per cent, declared that they had had this disease. Of the 50 patients found to have stones, 40 were asked as to an attack of typhoid fever in the past, and four said that they had had this disease. Therefore, of the 40 patients that had had gallstones four had had this condition subsequently to an attack of typhoid fever and 36 had gallstones without there being a history of such an occurrence in the past. It should be noted that of the 13 patients among the 259 questioned as to typhoid fever nine had had this disease, but had not developed gallstones subsequently. Therefore, twice as many cases that had had typhoid fever escaped gallstones as had had typhoid and developed them.

Several topics related to this investigation present themselves for comment.

TABLE I

500 CASES IN WHICH THE GALLBLADDER WAS EXAMINED BY PALPATION DURING OPERATION, GROUPED BY DECADES AND SHOWING INCIDENCE OF OCCURRENCE OF GALLSTONES

Decade	10–19	20–29	30–39	40–49	50–59	60–69	Totals
Gallbladders explored	4	100	195	152	33	16	500
Stones present	0	7	13	20	5	5	50
Approximate percentage of occurrence of stones	0	7.	6.25	13.	15.	31.	10.

TABLE II

OPERATIVE CONDITIONS IN 500 CASES IN WHICH THE GALLBLADDER WAS EXAMINED BY PALPATION DURING OPERATION

The Uterus: Uterine fibroids	193
Uterine displacements, fibrosis of uterus, cancer of uterus, *etc.*	112
The Uterine Adnexa: Ovarian cysts, inflammations of the tubes, tubal pregnancies	102
Other Conditions: Incisional and umbilical herniae, cancers of the colon, exploratory operations	93

Palpation of the gallbladder through the operative abdominal incision, while often affording information of value to both doctor and patient, should be employed with restraint and limited to suitable cases.

Undoubtedly, with increasing familiarity with the procedure the disturbance to the patient in accomplishing it is reduced, and considerable skill is acquired both in appreciating stones that may be present or, on the other hand, and determining with a reasonable degree of confidence that there is none.

While it seems that a small and solitary round stone may remain in the gallbladder at times without either producing symptoms or effecting pathologic changes in the gallbladder wall, very few cases among all those in this group have entirely escaped the consequences of retaining their stones. Very good and numerous reasons can be presented for the removal of the gallbladder found to contain stones. There is high probability of the eventual development of trouble, which, as in one case, may come in the

form of an acute gangrenous gallbladder and as the first manifestation of the presence of the stones.

As the individual possessing gallstones grows older the risks of cholecystectomy increase, as does also the extent of the pathology involving the biliary system.

SUMMARY

The final disposition of the 50 cases found at operation to possess gallstones can be given as follows: Six received immediate treatment for their gallstones; eight died more or less promptly, 12 sooner or later returned for removal of their gallbladders; 12 were lost contact with after various periods of observation; and 12 remain under observation at the present time.

Only two cases are presented as presumably examples of symptomless gallstones, and these from a fairly large group of cases representing biliary disease in its milder, intermittent or even completely unassertive varieties.

Numerous cases of quiescent gallstones were discovered, varying greatly in duration and judged by the period of time elapsing between the occasion of the discovery of the stones and the last preceding attack, or a subsequent attack, or both.

A brief review of each of the individual cases composing the group, with details of interest, follows:

Five cases found to have gallstones had cholecystectomies at the time of the discovery of the stones.* Two cases were errors in diagnosis; two had gallbladder symptoms complicating their operative conditions; one had apparently never had symptoms caused by the existence of the gallstones.

Case 4.—G. W., age 23 at time of operation, September 19, 1921: Married and three pregnancies. Operation: Ventrosuspension, appendicectomy. The gallbladder, found to contain an assortment of stones, immediately removed. Owing to patient's age and the displacement of the uterus, the possible significance of 19 months of indigestion since the birth of her second child was not appreciated until the gallstones were discovered.

Case 7.—R. A., age 32 at time of operation, May 1, 1923: No typhoid. Married and five pregnancies. Diagnosis, chronic appendicitis, based upon four definite, though mild attacks, involving the right lower quadrant during the preceding two months. There had been no digestive symptoms between attacks and the presence of gallstones was not suspected until found at operation. Gallbladder and appendix removed.

Case 19.—L. F., age 35 at time of operation, November 26, 1927: No typhoid. Single. An exceedingly obese patient. Operation: Excision large ovarian cyst. Seven large gallstones discovered in the gallbladder, which was removed. As there had been no symptoms that could be related to the gallbladder, the stones could be regarded as coexistent or even symptomless.

Case 24.—R. B., age 36 at time of operation, July 19, 1929: Had typhoid. Married and two pregnancies. Exploratory celiotomy for large tumor arising from pelvis, thought to be cyst or fibroid. A six-months fetus, with hydramnios was found. The gallbladder was found to contain a large number of small stones, and was then suspected

* In making up a group of the cases found to have stones, numbers were assigned to the cases in the chronologic order of their discovery. These numbers are retained in the subdivisions of the group.

of being the cause of the lower abdominal pain, although uterine complications could not be excluded. Gallbladder removed.

Case 31.—M. S., age 23 at time of operation, October 22, 1931: No typhoid. Married and two pregnancies. Operation for what were believed to be symptom-producing adhesions in right lower quadrant following appendicectomy. Gallbladder found to contain stones. Review of the history makes it doubtful that the appendix was ever affected. Misinterpretation of the symptoms caused by the gallstones resulted in an error in diagnosis in each instance. Gallbladder removed.

One case, found to have a solitary gallstone, was treated by opening the gallbladder, removing the stone and closing the gallbladder at the time of the discovery of the stone.

Case 22.—M. C., age 49 at time of operation, March 23, 1929: No typhoid. Married and six pregnancies. Hysterectomy for uterine fibroids. The gallbladder was found to contain a solitary small stone. The gallbladder was opened, the stone removed, and the incision in the gallbladder closed with some difficulty because of a thin and friable wall. For the 12 years since the operation the patient has complained only of occasional spells of gastric acidity, with some gas. This condition had also been present for a year or so preceding operation. However, the symptoms described are insufficient either in degree or type to be definitely related to the gallbladder or to suggest a recurrence of the stone.

Eight cases found to have gallstones were lost to this investigation because of death, five of these dying within a month, two under two years, and one surviving over five years. Four had had no gallbladder symptoms, so far as known. One had gone 21 years without an attack and one for seven years. Two had had symptoms at intervals for 7 and 14 years, respectively, preceding discovery of the stones.

Case 14.—M. H., age 49 at time of operation, February 7, 1925: Married and one pregnancy. Operation for malignancy of the uterus. Gallbladder contained a large solitary stone. Patient died 20 months later, apparently never having had symptoms due to the presence of the stone.

Case 26.—C. L., age 56 at time of operation, September 9, 1930: Married and one or more pregnancies. Operation for cancer of cecum with obstruction. The gallbladder contained a solitary stone size of a hickory nut. So far as known there had been no symptoms in the past referable to the gallbladder, the patient dying four days after operation.

Case 29.—M. N., age 62 at time of operation, May 2, 1931: No typhoid. Married and two pregnancies. Exploratory celiotomy for cancer of the uterus, found to be inoperable. Gallbladder found to contain one and probably more stones. Upon inquiry into the patient's past it was found that there had been an attack of gallstone colic in 1910 which lasted two days, followed by jaundice. Patient died one month following operation, apparently having lived for 21 years, or more, without the recurrence of symptoms referable to the gallbladder.

Case 30.—M. S., age 46 at time of operation, September 21, 1931: Married and one or more pregnancies. Operation for fibrosis of uterus. Gallbladder found to contain a cluster of small stones. After operation it was learned that patient had had a definite attack of right upper quadrant pain, with vomiting, 14 years before, followed by other attacks at intervals. The discovery of the presence of the stones resulted in additions to the patient's past history that should have been on record before operation, but

were omitted because of the urgent symptoms that brought her to the hospital. Patient died of complications on second day following operation.

Case 32.—M. F., age 65 at time of operation, July 22, 1932: No typhoid. Married and two pregnancies. Operation: Excision of malignant cyst of left ovary. Gallbladder contained 12 or more small round stones. Patient lived five months without gallbladder symptoms, nor had there been, so far as is known, any such symptoms at any time in the past.

Case 40.—C. G., age 62 at time of operation, June 3, 1935: Married, and one or more pregnancies. Operation: Cecostomy for malignancy of ascending colon with obstruction. Upon palpation, the gallbladder was found thickened and contracted about three round stones. Patient survived operation six days, and autopsy confirmed the observation made at the time of operation, three large stones being disclosed. A past history of seven years of indigestion that had not seemed particularly relevant before operation was thus probably accounted for.

Case 45.—K. O'C., age 34 at time of operation, August 17, 1936: No typhoid. Married and five pregnancies. Operation: Excision of cancer of cecum, and anastomosis. A stone the size and shape of a small olive felt in the gallbladder. Patient died on the 8th day after operation. The presence of the stone was confirmed at autopsy, the biliary passages being open and apparently normal. Apparently the only symptoms complained of had been those ascribed to the developing tumor of the large bowel.

Case 46.—F. K., age 62 at time of operation, May 6, 1937: No typhoid. Married and no pregnancies. Hysterectomy for adenocarcinoma of the uterus. The gallbladder was found to contain two marble-like stones. Inquiry after operation revealed that for a period of two years, beginning some five years previously, there had been several typical attacks of biliary colic. The patient died in July, 1942, there having been eight years without symptoms, three before and five after operation.

Twelve cases found to have gallstones subsequently came to cholecystectomy, having sooner or later developed acute symptoms—four during the first year following the discovery of the stones, four during the second year, and four at intervals of 8, 6, 5 and one-half and 2 years and ten months, respectively.

Case 8.—R. G., age 28 at time of operation, May 8, 1923: Had typhoid. Married and one pregnancy. Operation for excision of large ovarian cysts. Gallbladder found to be packed with stones. After two years patient developed acute gallbladder symptoms and cholecystectomy was performed elsewhere.

Case 10.—S. C., age 22 at time of operation, December 21, 1923: No typhoid. Married at 15, three pregnancies. Operation for advanced bilateral adnexal disease. Gallbladder felt to be filled with stones. A period of three years without symptoms was followed by five years of severe intermittent attacks. Cholecystectomy, October 5, 1931, eight years after discovery of the stones.

Case 11.—L. A., age 51 at time of operation, March 13, 1924: No typhoid. Married and ten pregnancies. Hysterectomy for uterine fibroids. Gallbladder contained numerous stones. Patient ridiculed the announcement as to the presence of stones, disclaiming all symptoms. Nine months later developed first acute attack. Attacks recurring, the gallbladder was removed November 29, 1925.

Case 12.—B. C., age 29 at time of operation, November 29, 1924: No typhoid. Married and one pregnancy. Operation for excision of ovarian cyst. Gallbladder found to contain numerous stones. Following operation it was learned that patient had been under medical care for mild but persistent indigestion for some time. Chole-

cystectomy March 10, 1925, with most satisfactory results. Nineteen stones found in the gallbladder.

Case 15.—L. H., colored, age 51 at time of operation, May 4, 1926: No typhoid. Married and one pregnancy. Hysterectomy for large uterine fibroid. A large solitary stone felt in ampulla of gallbladder. Three months after operation digestive symptoms developed. After another eight months attacks of pain came on and increased. Cholecystectomy March 13, 1928.

Case 27.—H. H., colored, age 22 at time of operation, October 20, 1930: No typhoid. Single. Operation for excision of large ovarian cyst. Several stones felt in the gallbladder. Two years after operation there was pronounced fat intolerance. During next four years digestive disturbances greatly increased. Cholecystectomy October 26, 1936, six years after the discovery of the stones, with great benefit.

Case 36.—H. B., age 37 at time of operation, March 13, 1924: No typhoid. Married, no pregnancies. Operation for excision of large ovarian cyst. Gallbladder felt tense but no stones were detected. An incisional hernia was repaired May 17, 1930, the gallbladder was not explored. On January 22, 1934, ten years after the first operation, the hernia was again repaired and a stone the size of a marble discovered in the gallbladder. The gallbladder was removed, July 31, 1934, following an acute episode of typical symptoms, with jaundice.

Case 38.—M. K., age 37 at the time of operation, June 11, 1934: No typhoid. Married and 12 pregnancies. Repair of a rather large epigastric hernia. Sole complaint had been the swelling of 12 years duration. The gallbladder contained many small stones. Following operation it was learned that during the last pregnancy, terminating three months previously, patient had been slightly jaundiced. Patient soon developed crampy epigastric pains radiating to the back, and fat intolerance. The gallbladder was removed September 27, 1934, and contained 89 faceted stones.

Case 39.—A. O., age 54 at time of operation, August 23, 1934: No typhoid. Married and three pregnancies. Repair of perineum and ventrofixation. Several faceted stones discovered in gallbladder. Six months later patient developed attacks of upper abdominal pain, and these increasing, the gallbladder was removed May 15, 1935.

Case 42.—J. M., age 43 at time of operation, August 13, 1935: Had typhoid. Married and no pregnancies. Operation for obstructing postappendicectomy adhesions. Several large faceted stones felt in the gallbladder. Six months later there was recurrence of abdominal pains, but without obstruction and presumably of gallbladder origin. Gallbladder removed February 4, 1937, with most satisfactory results.

Case 44.—F. S., age 61 at time of operation, May 27, 1936: No typhoid. Single. Hysterectomy for cancer of the body of the uterus. A number of small stones felt in the gallbladder. So far as could be determined patient never had gallbladder symptoms until the onset of an acute attack three days before the second operation, April 28, 1938, when a gangrenous gallbladder was removed filled with *Streptococcus viridans* pus and disintegrated stones. Recovery.

Case 47.—E. H., age 37 at time of operation, August 28, 1937: No typhoid. Married and one pregnancy. Salpingectomy for chronic pelvic inflammatory disease following her confinement in March, 1936. Gallbladder contained numerous small stones. There had been digestive symptoms for several years preceding the pregnancy. Seen at intervals for five years; patient continued to complain of general abdominal pains, which finally developed into definite attacks of gallbladder colic. After six months of attacks, that increased in frequency and intensity, the patient submitted to cholecystectomy March 13, 1943.

Twelve cases found to have gallstones were sooner or later lost contact with. Six were free from gallbladder symptoms when last seen. Two of these had been followed for five years or more; two for four years; the other two

for three and one-half years and ten weeks, respectively. Three were having symptoms when last seen, and three disappeared too promptly after the discovery of the stones to permit observation.

Case 2.—C. G., age 40 at time of operation, June 4, 1921: Married and eight pregnancies. Operation for excision of large ovarian cyst. Gallbladder found filled with stones. Inquiry into patient's past history failed to elicit complaints that might be referred to the gallbladder. Patient could not be found following completion of convalescence.

Case 3.—V. C., age 40 at time of operation, August 6, 1921: Married and seven pregnancies. Hysterectomy for uterine fibroids. Gallbladder felt to contain stones. Upon investigation following operation it was learned that patient had had occasional attacks of epigastric pain, presumably, but not too clearly, due to her gallbladder. Could not be found following completion of convalescence.

Case 5.—V. A., colored, age 38 at time of operation, February 25, 1922: Married and one pregnancy. Hysterectomy for an unusually large uterine fibroid. Gallbladder was found to contain eight stones. History had recorded frequent belching of gas which was attributed to, and may have been due to the presence of the abdominal tumor. Patient was followed for five years after operation, without occurrence of gallbladder symptoms during this period.

Case 9.—M. B., age 43 at time of operation, May 31, 1923: Married and ten pregnancies. Operation for repair of umbilical hernia. A solitary round stone the size of an ordinary marble was found in the gallbladder. For one year preceding operation patient had complained of abdominal pain, which was attributed to the hernia, and presumably correctly so since patient was followed for four years after operation without occurrence of gallbladder symptoms before being lost sight of.

Case 13.—C. M., colored, age 41 at time of operation, January 27, 1925: Single. Hysterectomy for large uterine fibroid. Gallbladder found to contain a large stone impacted in the ampulla. Two years of increasing indigestion and attacks of abdominal pain had been attributed to the large and growing tumor. There was relief of symptoms for six months after operation and then recurrence with greater severity. After nine months of persisting symptoms patient finally agreed to operation, and then suddenly disappeared.

Case 18.—F. H., age 46 at time of operation, April 9, 1927: No typhoid. Married and five pregnancies. Hysterectomy for fibrosis of uterus. Gallbladder was found to contain a large solitary stone and probably smaller stones. Inquiry revealed that patient had been jaundiced during her last pregnancy five years before. Six months after operation patient disappeared for nearly ten years, reappearing in April, 1937, because of a prolapse. At this time she was having, and had had for the past six months, indigestion, gas and fat intolerance, and inability to manage a full meal. Refusing cholecystectomy, the prolapse was repaired. After ten months, free of all symptoms, she again disappeared.

Case 20.—M. P., age 48 at time of operation, April 7, 1928: No typhoid. Married and one or more pregnancies. Hysterectomy for uterine fibroids. The gallbladder contained numerous small stones, mostly in the ampulla. Inquiry after operation failed to establish a history of attacks of pain or digestive symptoms that might be due to the presence of the stones. Patient disappeared at the termination of her convalescence.

Case 21.—C. R., age 43 at time of operation, September 27, 1928: Married and three pregnancies. Typhoid fever when 13 years of age. Operation for repair of incisional hernia in lower abdomen. Two small faceted stones were felt in the gallbladder. During the following five and one-half years there were no symptoms suggestive of the presence of the stones. The patient disappeared upon recommendation of an operation for recurrence of the hernia.

Case 25.—M. W., colored, age 32 at time of operation, July 25, 1929. No typhoid. Married and two pregnancies. Hysterectomy for large uterine fibroid. The gallbladder contained numerous medium-sized faceted stones. Patient was followed for three and one-half years before being lost contact with and during this period was entirely free from symptoms and without need of restrictions in diet.

Case 28.—J. B., colored, age 35 at time of operation, February 28, 1931: No typhoid. Married and no pregnancies. Hysterectomy for uterine fibroids. A solitary stone found in the gallbladder, size of a marble. Past history was irrelevant. Thirteen years before there had been a gynecologic operation, the gallbladder presumably was not investigated. Patient was followed for over a year, gaining in weight but complaining of flatulence, possibly related to her gallbladder.

Case 33.—G. H., colored, age 42 at time of operation, February 2, 1933: No typhoid. Married and no pregnancies. Hysterectomy for uterine fibroids. The gallbladder was thickened and contained a large number of stones. There had been acute attacks of lower abdominal pain thought to be due to intestinal adhesions, which were found to be extensive at operation. Fourteen years previously the patient had been operated upon for adnexal disease, the gallbladder apparently was not explored. Patient was free of all symptoms when last seen, ten weeks after the discovery of the stones.

Case 41.—L. E., colored, age 40 at time of operation, July 18, 1935: No typhoid. Married and two pregnancies. Hysterectomy for uterine fibroids. A small round stone felt in the gallbladder, with probable additional smaller stones. When last seen, nearly four years after operation, there had been no symptoms that might be attributed to the gallbladder during this period.

Twelve cases found to have gallstones have continued under observation. Six of these have had one or more attacks of biliary disease or are having symptoms at the present time, this during periods of observations ranging from 4 to 15 years. Without regard to occurrences preceding the discovery of the stones, these cases seem properly to belong to the quiescent gallstone group.

The six remaining cases are believed to have had no symptoms during periods of observation of 20, 15, 13, 9, 3, and 3 and one-half years. Four of these have definitely had or cannot be said not to have had, symptoms prior to the discovery of the stones, and even though believed to have been symptom-free since, cannot be rated as cases of symptomless stones but are added to the quiescent gallstone group.

Two of these 12 cases can be said to have had no symptoms before the discovery of the stones with considerable assurance. They may be accepted as cases of symptomless gallstones, if such exist. One of these was operated upon at the age of 38 and followed for 15 years, and one at the age of 49 and followed for nine years.

Case 1.—A. H., age 30 at time of operation, July 5, 1918: No typhoid. Married and five pregnancies. Ventrosuspension for posterior displacement of the uterus. A small number of faceted stones were felt in the gallbladder. While this patient was of a thin and nervous type and had innumerable complaints, none of which could be assembled to form a picture of any one thing, it has been impossible to ascertain that during a period of over 20 years there have been symptoms that could be definitely attributed to the gallbladder.

Case 6.—S. W., age 43 at time of operation, March 24, 1923: No typhoid. Married and three pregnancies. Operation for excision of ovarian cyst. Gallbladder felt to

contain two medium-sized faceted stones. It was learned after operation that four years previously and three days after the birth of her last child, there had been a definite gallbladder attack, with jaundice. There have been two attacks without jaundice at intervals of five and ten years since the discovery of the stones. There has been no attack during the past three years.

Case 16.—A. W., age 38 at time of operation, August 18, 1926: No typhoid. Married and two pregnancies. Salpingectomy for ruptured ectopic. Gallbladder found to contain a stone the size of a marble, with several smaller stones. Owing to a misunderstanding with the family physician the patient was not informed as to the discovery of the stones for 15 years. When finally told of their presence, she stated that she was then and always had been in perfect health, asked as to the location of the gallbladder and what would be the characteristic symptoms should these appear.

Case 17.—A. M., age 45 at time of operation, March 3, 1927: No typhoid. Single. Hysterectomy for uterine fibroids. Gallbladder contained six or more very small stones. Patient was free from symptoms for nine years, then for one year was annoyed by gas and bloating and occasional crampy pains across upper abdomen. There has been no recurrence of these symptoms for the past five years.

Case 23.—C. H., age 52 at time of operation, April 27, 1929: No typhoid. Married and three pregnancies. Operation, salpingectomy with ventrosuspension. The gallbladder was felt to contain a small, solitary nonfaceted stone. The patient was seen a year after operation and then disappeared for twelve and a half years, returning thirteen and a half years after the discovery of the stone because of a breast tumor. She had had no symptoms that would indicate a disturbance caused by her gallstones.

Case 34.—M. M., age 49 at time of operation, April 4, 1933: No typhoid. Married and two pregnancies. Hysterectomy for uterine fibroids. Gallbladder contained a round stone and a number of smaller stones. Patient had had no symptoms referable to the gallbladder prior to operation, and has been entirely free from all such symptoms for more than nine years since.

Case 35.—A. W., age 35 at time of operation, October 3, 1933: Married and one pregnancy. No typhoid. Ventrosuspension. Gallbladder was felt to contain a considerable number of small stones. Eighteen months after operation patient developed digestive symptoms, chiefly gas and fat intolerance, regularly brought on by indiscretions of diet. These symptoms have persisted in variable degree for ten years, to date.

Case 37.—I. C., age 28 at time of operation, May 24, 1935. No typhoid. Married and three pregnancies. Gallbladder found to contain a round stone the size of a marble, with additional smaller stones. Three years after operation patient gradually developed digestive symptoms, with fat intolerance, which persisted for more than two years. The past year has been entirely symptom-free.

Case 43.—M. P., age 36 at time of operation, April 8, 1936: Married and two pregnancies. Ventrosuspension for posterior displacement of uterus. A very small and apparently solitary stone felt in the gallbladder. Six months following operation patient had a definite attack of biliary colic followed by two other attacks during the succeeding 12 months. There have been no recurrences during the past four years.

Case 48.—M. H., age 48 at time of operation, January 19, 1938. No typhoid. Married and one pregnancy. Gastro-enterostomy for pyloric obstruction. Symptoms had been typical of the gastric condition present. A faceted stone, apparently solitary, was felt in the gallbladder. Operation relieved all symptoms, the gallstone apparently having played no part in them. The patient has been in excellent health for three years, having gained in weight and general condition and remained free of all complaints.

Case 49.—G. D., age 48 at time of operation, February 18, 1938: No typhoid. Married and no pregnancies. Hysterectomy for uterine fibroids. Gallbladder found to contain one faceted stone one-half inch in diameter and numerous other small stones. The patient when informed of the presence of the stones stated that she had had indigestion for years. Fourteen months after operation fat intolerance developed, with

tendency to nausea and inability to manage full meals. These symptoms persisted for two years, and were followed by a year of greatly improved general health. When last reporting patient stated that she had not been so well in the past five years.

Case 50.—L. K., age 49 at time of operation, April 9, 1938: No typhoid. Married, three pregnancies. Hysterectomy for uterine fibroids. There were several small faceted stones in the gallbladder. Operation was delayed for some months because of attacks of epigastric pain, suspected of being of cardiac origin. This was not substantiated nor has it been since operation, which was followed by complete relief of symptoms. There have been three and a half years without symptoms which are now believed to have been due to the gallstones.

REFERENCE

[1] Truesdell, Edward D.: Incidental Gallstones in Women. ANNALS OF SURGERY, **98**, 362, September, 1933.

PREOPERATIVE MEASURES USED IN WAR SURGERY IN CHINA: WITH SPECIAL REFERENCE TO THE DELIMITING TOURNIQUET*

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IT IS OUR PURPOSE to outline some of the preoperative measures which we found useful in taking care of casualties in connection with our experiences in the early part of the Sino-Japanese War (January, 1938, to January, 1941). These casualties were treated in four different North China mission hospitals on both sides of the fighting lines. They were seen on the average of two or three days after wounding, but this varied considerably. Some were seen immediately. Unfortunately, our records have been lost to the enemy and hence are unavailable. In general, we found that preoperative preparation of the patient was just as important as in civilian surgery, if not more so. The form it took, however, differed according to the time that had elapsed after injury and the circumstances under which we worked.

Shock.—We were, unfortunately, not in a position to use the best methods in treating shock, for blood and plasma were not available except as donated by our own overworked staff. In consequence of this, only the most exsanguinated could have transfusion. If we had it to do over again, we would certainly press propaganda to the point where stored blood or plasma would be available in sufficient quantity, at least while we were working in Free China. At any rate we did not encounter any deaths from injection of too much plasma (or too much of the contained sodium citrate), such as has been reported recently by Drummond[1] and Ivy, and his collaborators.[2] We did give morphine subcutaneously, and saline and glucose intravenously as indicated, but we saw lives lost both in the initial shock following war trauma and postoperatively through lack of suitable intravascular fluid such as blood or plasma.

Exhaustion.—In the autumn of 1938, 33 Chinese stretcher casualties were landed on us all at once. Because of lack of space in our reception rooms for so great a number of stretcher cases, they were seen in a preliminary way as they were lined up on the tennis court. As we went from stretcher to stretcher, a composite picture was seen of utter exhaustion, malnourishment and fever. They had been wounded in fighting the Japanese about 140 miles away and had been carried westward for eight days by litter-bearers over rugged mountain passes to reach our hospital. Very few inns had been encountered along the way and the food and lodging which had been obtained was only of the coarsest variety. There had been no immobilization of wounded parts and no dressings en route. Their wounds were almost all

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FIG. 1.—Single transverse line: Level of proposed amputation (upper thigh).
Double transverse line: Level of application of the delimiting tourniquet.
Stippled area: Area of gangrene induced by tourniquet.
Black-shaded area: Original area of gangrene and infection.

badly infected and many were infested with maggots (indicating an extreme degree of contamination, no matter what may be said for the therapeutic value of the maggots!).

In a few of these cases we yielded to the temptation of operating right away and the results were decidedly disappointing, even with amputations for cutting away severely infected and gangrenous parts. Exhaustion and malnutrition had prepared them for the worst postoperative shock and stormy convalescence.

The rest of our 33 casualties, we kept in the ward for a week or more before undertaking the indicated operations. It was remarkable to see the preoperative improvement that came over them with a comfortable bed, congenial surroundings, immobilization of the wounded part by the simplest means; *e.g.*, a Thomas splint with adhesive traction, supplemented in many instances with sulfanilamide by mouth, vitamins and good nourishing food. Practically all of these patients did very well on the operating table and thereafter. Thus, we learned that it is far more necessary to give rest and nourishment to such casualties than to undertake a spectacular and hurried operation. We later discovered that Keen[3] had stressed this matter in his book on war surgery in the following statement:

"The wounded will often have suffered from loss of blood, loss of sleep, insufficient food, and exposure to cold, and if to these are added severe pain and the exhaustion due to an unavoidable jolting transportation, they will be on the verge of collapse. The first needs of such a man are rest, warmth and food. . . . These restoratives may easily be required before any treatment (save for hemorrhage) should be attempted. 'The more experienced the surgeon, the less is he likely to hurry on a severe primary amputation.' Threatened gas gangrene or rapidly spreading sepsis may force his hand. Much discretion, therefore, must be allowed the surgeon."

Malnutrition.—A great deal of inanition was seen among troops who, at best, were getting along on inadequate diets. Particularly was this true of the Chinese Communist Troops who practiced extreme Marxism, with its share-alike principles applied equally to civilians and military personnel, resulting disastrously in view of prevalent conditions bordering on famine. When these men became wounded, the problem seemed to be primarily one of hypoproteinemia and avitaminosis. Feeding them good nourishing food, rich in protein,[4] and, in the more extreme cases, the administration of ascorbic

acid parenterally,[5] seemed to play a big rôle in preoperative preparation and recovery.

Infection.—In many instances infection was inevitable in our war wounds, particularly in those which were seen late. We started using sulfanilamide tablets in January, 1938, when we received our first consignment of 3000 tablets. Sulfanilamide and small quantities of sulfapyridine were the only sulfonamides obtainable during the period under consideration, *viz.*. up to January, 1941. Sulfonamide powder, moreover, was not used locally because it had not become available in sufficient quantity. As a preoperative measure, saturation of the body tissues with sulfanilamide was usually accomplished by the administration of the drug orally (0.67 to 1.0 Gm. every four hours), or, when speed was required by reason of coma or severity of infection, intravenously (500 cc. of one-half per cent sulfanilamide in physiologic saline, followed by 200 cc. every four to six hours), for at least 24 hours before operation. In our experience this decidedly cut down the amount of post-operative reaction.

Intercurrent Disease.—Another thing that we encountered frequently was the casualty who had been holding the balance of power against latent disease, such as malaria. In the face of trauma and exhaustion, latent malaria tended to develop into clinical malaria, as demonstrated on frequent occasions by blood smear. Accordingly, when the temperature rose in our casualty cases, quinine was often just as likely to be needed as a sulfonamide. We frequently had to give both at once, as a matter of fact. It is particularly precarious to have a malarial chill superimposed upon postoperative shock.

Toxemia.—In some cases seen several days after injury, the insult of toxemia was added to that of malnutrition and infection. Our experience with the use of what we might call, for want of a better term, the delimiting tourniquet,[6, 7] would lead us to say that we believe that there is a very definite field for the use of the tight gum rubber tubing tourniquet to prevent absorption of toxic products from a severely septic and/or gangrenous extremity which will later require amputation. Gangrene and infection elaborate toxins by reason of tissue disintegration and bacterial growth. The resulting toxemia produces disturbed body metabolism. Should toxemia become severe enough, a comatose stage is reached which, if the toxemia continues unabated, eventually becomes irreversible and fatal. It is at the comatose stage that we have seen dramatic restoration of normal metabolism by the simple expedient of applying a tight tourniquet well above the affected area with a view to later amputation at this level or higher. The application of the delimiting tourniquet is promptly available in warfare in many places where freezing of the affected extremity, the beneficial effects of which have been demonstrated by Allen[8] and McElvenny,[9] is not.

The Rationale of the Delimiting Tourniquet.—There appear to be two principal indications for the delimiting tourniquet. In the first place there is sometimes the need of preoperative improvement before subjecting the patient to amputation; and, secondly, there is the inevitable delay in getting the

severely toxemic casualty, who may have been lying out on the battlefield for two or three days, to a hospital. The tourniquet is applied distal to the anticipated level of amputation but sufficiently proximal to the diseased part that it is well above any area of infection. We would like to stress this particular point, for the application of the delimiting tourniquet to any part of the limb where there may be deep infection helps to further confine the products of inflammation.

In view of the fact that a previously reported case of our use of the delimiting tourniquet for gunshot wound is rather inaccessible at present, having been published in China shortly before America entered the war,[6] it might not be amiss for us to give a brief summary of it, since it so well illustrates the usefulness of this procedure.

ILLUSTRATIVE CASE IMPROVED BY THE DELIMITING TOURNIQUET

Case Report.—A Chinese official, age 26, was admitted to our hospital with a history of a gunshot wound in the posterior aspect of the lower third of the right thigh four days previously. On the day of injury and the following day, an orange-colored Chinese corrosive powder had been introduced into the tract of the missile. Previous experience had taught us that this corrosive powder continues to exert a necrosing action similar to phenol over a matter of many days. The next day the skin about the wound had turned black in color. On admission, the posterior aspect of the lower third of the right thigh was found to be gangrenous and an extensive slough was cut away without pain, followed by the outpouring of a serosanguineous fluid mixed with globules of fat. An area in the upper part of the calf of the right leg appeared to be threatened with gangrene, and the dorsalis pedis artery was not palpable on that side. Gangrene set in subsequently and gradually spread to include the entire right leg below the knee.

Eight days after admission, the gangrenous limb had so affected the patient's condition that he became unconscious. The following note was written on his chart that day: "Condition is so poor this morning that, while full consent for amputation has at last been obtained, it seems worthless. A tourniquet is being applied to keep poisons from going back to the heart as a preferable alternative." The tourniquet was applied tightly around the upper thigh.

Up to the day of the application of the tourniquet, the temperature of the patient had become steadily higher, having ranged between 103° and 104.8° F. for the four days preceding. On the morning of the following day, 24 hours after the application of the tourniquet, the temperature had fallen to 100.4° F. The patient was again conscious, with some appetite for food, and was demanding amputation, but as the relatives were not unanimous at that time, it was not undertaken. Twenty-eight hours after the application of the tourniquet, the temperature again rose, this time to 105.4° F. His condition became steadily worse until death ensued 53 hours after the application of the tourniquet. Our feeling was that this patient had so improved that he would have stood amputation better 24 hours after the application of the tourniquet than before.

Precautions in the Use of the Delimiting Tourniquet.—It is of course necessary to see that the delimiting tourniquet is not released until amputation is performed. We are aware that this, at first sight, seems to contravene some of our present U. S. Army directives as regards the frequent loosening of the tourniquet. It must be remembered, however, that these directives refer

to the control of hemorrhage. We feel that the use of the tourniquet for controlling toxemia belongs in a very different category. Our suggestion is that when the delimiting tourniquet is applied, it should be extensively covered with adhesive tape which is appropriately labelled, indicating that it is not to be removed.

Subsequent experience with two other cases in addition to the one reported above makes us inclined to recommend reapplication of the delimiting tourniquet every 24 hours at a slightly higher level each time, until amputation is performed, so as to avoid contact of normal tissue with toxic fluids produced by pressure necrosis at the point of application of the tourniquet. Our reason for suggesting 24 hours as the time limit is that we noted a sharp rise of temperature soon after the lapse of 24 hours in those cases where we did not reapply the tourniquet at a higher level. On the other hand, Maxeiner[7] apparently did not resort to reapplication at a higher level and his results were seemingly as good. Whether more rigid attention to tightening the tourniquet *in situ* would have accomplished the same thing in our cases, we do not know.

In reapplying the tourniquet, the old tourniquet is left in place until another tourniquet has been applied proximal to it. It is applied as tightly as possible. At the end of several hours it usually produces a very deep indentation in the soft tissues, often with obvious local liquefaction necrosis.

Ordinarily, if the delimiting tourniquet is applied when the patient is in coma, there is no pain nor discomfort even after full consciousness returns. If the tourniquet is applied (or reapplied) when the patient is not comatose, there is a very painful reaction for which morphine should be administered beforehand. After the first hour or two there is no pain, since the tourniquet produces anesthesia by that time. We do not feel that the patient need necessarily have advanced to the comatose stage in his toxemia before the delimiting tourniquet is first used. Nevertheless, his condition must obviously be severe enough to require amputation before resorting to this procedure.

Conservative Treatment for Gas Gangrene.—Gas gangrene gave disappointing results in our earlier cases where we did immediate amputation. The use of conservative measures with delayed amputation or no amputation at all, seemed to give the best results. Sulfanilamide was administered, intravenously the first day in our serious cases, after which it was given orally. This seems justifiable, largely on the basis that the sulfonamide counteracts the symbiosis of streptococci with gas gangrene bacilli.[10] In our four cases seen in 1940, amputation was deferred and we were able to carry them through to a successful issue despite the fact that we did not have antitoxic serum for gas gangrene available. They received no local treatment aside from establishment of drainage in the simplest manner, changes of dressings and immobilization, as indicated. Thus, amputation was postponed for several weeks even though they were very toxic. In half the cases amputation did not prove necessary whereas in the other half we were able to

perform a more conservative amputation than would have been otherwise possible.

The Delimiting Tourniquet for Gas Gangrene.—On further reflection, we are inclined to say that the delimiting tourniquet might find a useful field in the treatment of gas gangrene in cases where eventual amputation will be required, although we did not actually use it in our cases. Our reason for this suggestion is that these patients are extremely toxic. Reimers,[11] furthermore, reports the successful use of a tourniquet under somewhat similar circumstances:

"In cases in which gas gangrene has already set in, and serious damage from injuries requiring amputation is present, the author recommends an immediate tourniquet bandage at the point of the intended amputation. He has never seen gas gangrene spread beyond the point of the tie-off."

Maxeiner[7] also expresses a similar viewpoint by implication when, in the discussion of one of his cases, he says:

"Gas bacillus infection . . . certainly would not have occurred if, in our eagerness to conserve all possible tissue, we had not placed our tourniquet too low."

COMMENT.—These procedures for improving the conditions of our casualties before operation doubtless differ somewhat from those which are used on other battle fronts. Certainly intravenous plasma and blood are being utilized elsewhere more than we used them. In general, however, the problems of shock, exhaustion, malnutrition, infection, intercurrent disease, toxemia and gas gangrene remain the same, although their relative importance may vary. No substitute can be found for good surgical judgment in their solution. The delimiting tourniquet should play a life-saving rôle in some instances, but its implication; namely, inevitable amputation, must be constantly borne in mind.

SUMMARY

Our experiences with methods for improving the condition of our casualties in China have been recounted, especially in regard to shock, exhaustion, malnutrition, infection, intercurrent disease, toxemia and gas gangrene. The rôle of intravenous fluids, rest, protein-rich diet, ascorbic acid, sulfonamides, specific treatment for intercurrent disease, and the delimiting tourniquet, as preoperative measures, is outlined. In particular, the effects of the delimiting tourniquet are discussed and an illustrative case is presented.

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CYSTOMYOMA OF SEMINAL VESICLE*

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THE RARITY of this lesion warrants description and discussion of every case. To our knowledge, no such observation has been reported in the Anglo-American literature.

Case Report.—Hosp. No. 152951: M. L., white, male, age 66, was admitted to the Beth Israel Hospital, May 6, 1943, because of a palpable mass in his left lower abdominal quadrant, which had been noticed two months previously. It occasioned him no pain or discomfort and he was not aware of its presence. The mass had not increased in size since it was discovered. There had been no abnormal gastro-intestinal symptoms. Appetite had been good, bowels regular, no blood had been noticed in the stool. There had been no weight loss, no dysuria, nocturia, hematuria or urgency. Neither had there been any symptoms of loss of cardiac reserve, the patient having carried on his usual occupation without interruption.

Physical Examination: The patient was thin, lungs clear to auscultation and percussion, pulse 80, regular sinus rhythm, no murmurs heard, blood pressure 138/80. The abdomen was scaphoid, soft, not distended. The liver edge was palpable 5 cm. below the costal margin; it was sharp and smooth. The spleen was not palpable. In the left lower quadrant there was an irregularly, round, hard nodular mass, about 8 x 8 cm. in diameter. It was movable but not freely so, and not tender. Rectal examination revealed no intrinsic lesion. Bimanual palpation with one finger in the rectum and the other hand on the abdomen demonstrated that the mass extended into the pelvis, almost completely filling it. It was fixed and immovable in the pelvis, but pressure by the abdominal hand was transmitted through the mass to the rectal finger. The prostate was in normal position and of normal consistency.

Barium enema showed no intrinsic colonic lesion, but the rectum and sigmoid were pushed to the right by the mass filling the pelvis.

Laboratory Data: Red blood cells 4,600,000, hemoglobin 88 per cent, white blood cells 6,200, with 69 per cent polymorphonuclear leukocytes. Urine: Specific gravity 1.012, glucose negative, albumen faint trace, white blood cells 18-20 per H. P. F., numerous urates.

Clinical Diagnosis: The original diagnosis rested between carcinoma of the rectum, with pelvic involvement; and retroperitoneal tumor, possibly fibrosarcoma or neurofibroma.

Operative Pathology: May 11, 1943 (Dr. Standard): The sigmoid was pushed to the right by a retroperitoneal, lobulated, hard mass which filled the pelvis and the entire hollow of the sacrum, pushing the bladder anteriorly. Portions of the tumor were cystic and these cysts contained dark, thick, chocolate-brown fluid. One such cyst was located deep in the hollow of the sacrum close to the area of the seminal vesicles, and the left vas deferens seemed to emerge from it. The entire tumor was well-encapsulated and could be enucleated along its lines of cleavage. The mass was roughly 15 x 13 cm. in diameter (Fig. 1).

Operative Technic: Left midline muscle-splitting incision. Rectus fascia was split and the rectus muscle displaced laterally. Peritoneum entered. Small intestine packed

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off under the upper angle of the wound. The posterior peritoneum along the left lateral surface of the tumor was incised and the tumor enucleated from its retroperitoneal bed. There was some spillage of dark brown fluid during the enucleation. There was a sharp line of cleavage between the major portion of the solid tumor and the cystic portion (3 x 4 cm.) which lay deep in the pelvis and from which the left vas deferens arose. The vas was ligated and cut from the cyst. (The other vas, which was found in the specimen, was not recognized during operation). The bladder was identified anteriorly and a catheter inserted. Clear urine was evacuated when the procedure was completed. Posterior peritoneum resutured over bed of tumor and abdomen closed in layers.

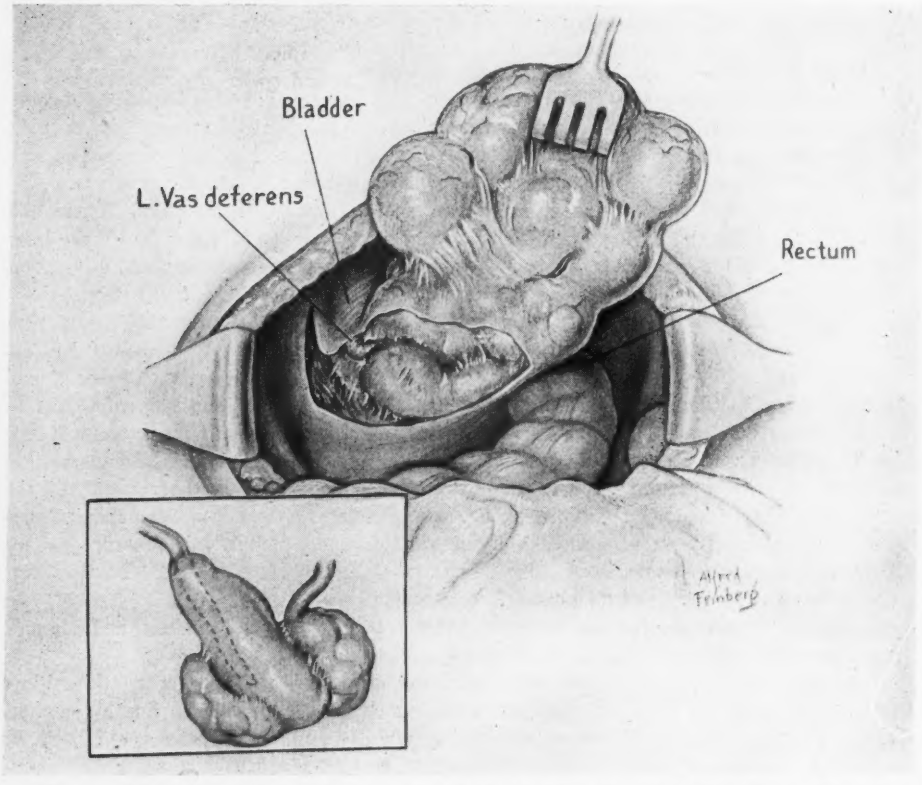

FIG. 1.—View of operative field (reconstructed), looking into the pelvis from above. Through a window in the posterior peritoneum one sees the left vas deferens and the adjacent cyst. The recto-sigmoid has been pushed towards the right by the tumor. The retractor has pulled the myomatous mass out of the abdominal cavity.

(Insert)—The dotted line indicates the course of the ductus deferens within the cyst wall.

Postoperative Course: Uneventful. Wound healed *per primam.* Patient discharged 13 days after operation.

Follow-up: Three weeks after operation the patient reported noting "blood in his urine." The urine was brown; microscopically, it showed no red cells. The color of the urine was due to the same brownish, thick material which had been originally evacuated from the tumor. Only on two occasions, a few days apart, did the patient notice this discoloration of the urine.

Today, more than five months after operation, the patient is in perfect health.

Pathologic Examination.—Gross: No. 43184: The specimen was irregularly lobulated and firm. It consisted essentially of one somewhat kidney-shaped piece, 14 x 11 x 8

cm., which was connected to another irregularly ovoid piece, 8.5 x 6 x 6 cm., by means of a pedicle-like structure. The specimen was surrounded by a hyperemic capsule in which many larger and smaller blood vessels were seen. Hyperemic membranous flaps were loosely attached to the outside. The one surface of the larger ovoid piece

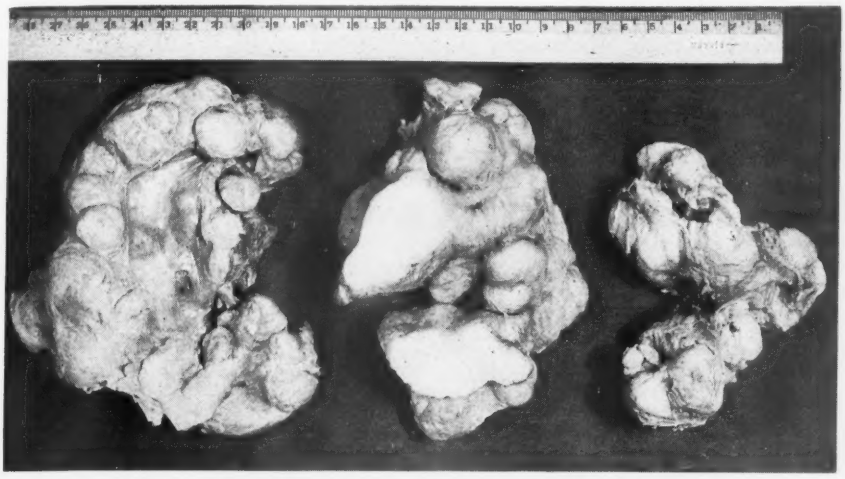

FIG. 2.—Gross specimen after fixation. Note the characteristic round myomatous nodules. The whitish areas in the middle specimen correspond to recently made cut-surfaces. The cavity is visible in the largest piece.

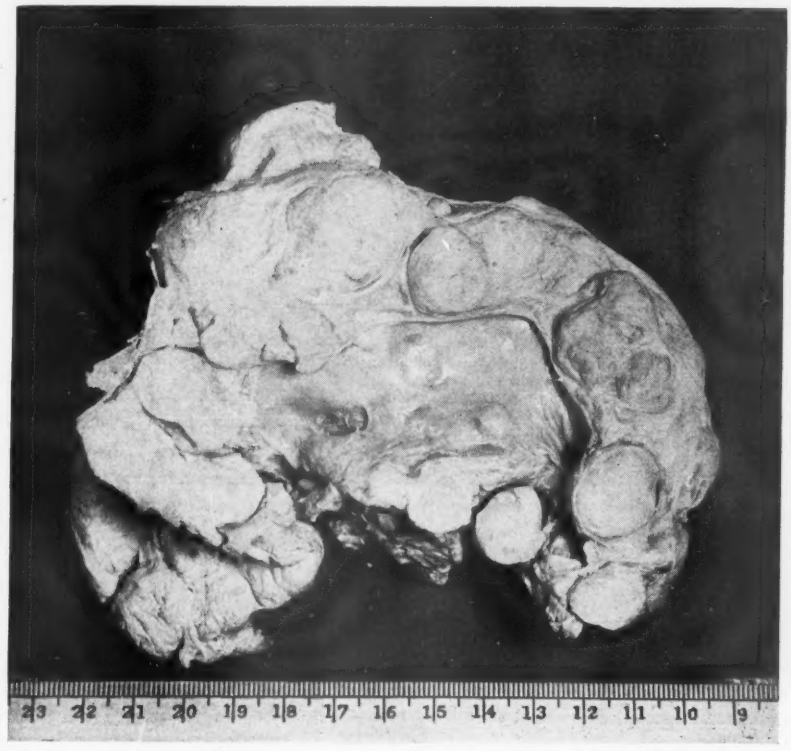

FIG. 3.—Close-up of largest piece. The high lights indicate the smooth lining in the cavity.

was flat, the other one irregularly convex. Both pieces were subdivided by grooves between which irregularly ovoid portions of different sizes protruded. A long section through the larger piece clearly showed many, more or less completely separated, nodules. The cut-surfaces could best be described as being very similar to those of myoma uteri.

Near the convex surface of the large piece a cavity was situated. Its volume was about one-fourth of the whole piece. It was crescent-shaped, it had a distinct smooth lining which was sharply demarcated from the surrounding tissue. The cavity had prolongations whose outlines corresponded to the contours of the whole piece. A transverse incision into the smaller piece opened a similar smaller cavity. Both cavities contained rather thin, dark reddish-brown fluid. (Figs. 2 and 3).

FIG. 4.—Characteristic structure of mucosa of seminal vesicle. The lining of the cyst appears in the upper portion of the specimen as a thin, dark contour.

A flat, soft, hollow specimen, 9 x 4 x about 1 cm., was received separately. It had torn prolongations and two ovoid thickenings. From an opening at one end dark, brownish fluid exuded. The lining of the cavity was smooth, partly pale, partly deep red. One of the prolongations contained a continuation of the cavity, about 1.2 cm. wide. The other protrusion was a thin, firm, cylindrical structure with very narrow lumen and firm elastic, obviously muscular, wall. Both looked like vas deferens. The outer aspect of the ovoid thickenings was suggestive of seminal vesicle; the cut-surfaces were characteristic (see insert to Fig. 1). The one seminal vesicle-like structure measured 3 x 1.5 x 1 cm., the other one 3.5 x 2 x 1.3 cm. They were separated by a piece of cyst wall, about 1 cm. wide. The cylindrical structures which entered this specimen really were the vasa deferentia. They were normal in thickness and slightly tortuous. They entered the wall of the cystic structure at an acute angle and ran mostly in the wall, with their lumina very near the surface. The average width of the lumen was 2.5 mm. About one centimeter from the one pole of one seminal vesicle the lumen was somewhat widened. The probing of the ducts was done after fixation of the specimen. Through the one the probe passed easily, not through the other. There was, however, no reason to assume that the other duct did not communicate with the lumen of the cyst.

Microscopically, the picture of the solid tumor was that of fibromyoma. As is usual in such tumors, the ratio between muscle and connective tissue varied, and so did edema and inflammation, the latter not being severe anywhere. Elastic fibers were few except for the subepithelial layers. These layers ran parallel to the surface of the cavity and, thus, were more regularly arranged than the layers which formed the myoma proper. The subepithelial layers contained small amounts of light brown pigment. The cavity in the myoma was lined with a single layer of cylindrical cells. There were no glands. The cells did not contain mucin. Directly under the epithelium some large, obviously phagocytic, cells were situated.

In sections from different portions of the cystic specimen (Figs. 4 and 5) the microscopic pictures were those of seminal vesicle, ampulla or vas. The muscular walls of these structures were continuous. There was some pigment in epithelium and in muscle. Subepithelial phagocytic cells were present. There were a few calcifications in the mucosa. Sperm heads were found in the lumen. The characteristic subepithelial elastic structures were conspicuous.

Only four reports of such cases could be found; none in the English or American literature.

E. Emmerich, in 1910, reported the first one under the title "Enormous Cyst of Vas Deferens." The tumor was found accidentally during the autopsy of a 74-year-old man who had died of leukemia. No urologic symptoms had existed and no pelvic pain. Both seminal vesicles were normal, as were testicle and epididymis on both sides; the prostate gave the picture of ordinary

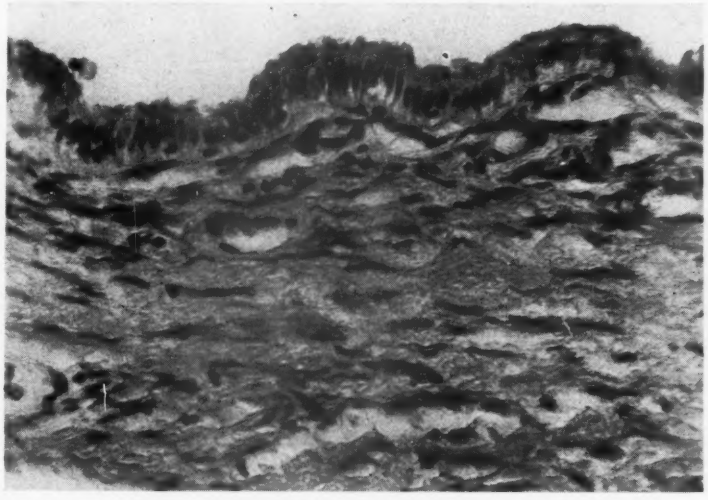

FIG. 5.—The cavity is lined with a single layer of regular high cylindrical epithelium.

hypertrophy. Right kidney and ureter were absent, there was no trace of a right ureteral opening in the bladder. The tumor (Fig. 6) arose from the left vas deferens, between ampulla and ejaculatory duct. It consisted of a round, firm, smooth, fist-sized mass which protruded from the small pelvis to the right of the midline. This mass was attached to the left ampulla towards the midline by means of a thick-walled hollow stalk, 6 cm. long. The lumen of the stalk communicated with the lumen of the ampulla and with the epithelium-lined cavity in the fist-sized mass. The wall of this cavity was only 2 mm. thick, that of the cylindrical portion was thicker; both consisted essentially of smooth muscle fibers. The epithelium was cylindrical or cuboidal. No spermatozoa were found.

Emmerich considered his case a cyst of the vas deferens, on the basis of a congenital malformation.

In 1912, Voelcker published a case of "Myoma of the Capsule of the

Seminal Vesicle"—this is the only case with clinical symptoms. Voelcker's patient was 56 years old; for more than 15 years he had suffered from pain in the perineum, he had consulted numerous surgeons, had been proctoscoped frequently, had been subjected to various procedures with no avail, and had, finally, become a morphine addict. On rectal examination a nontender swelling could be felt above the prostate. On bimanual palpation, in Trendelenburg position, under general anesthesia, it appeared as a movable, firm, smooth, spherical mass in the region of the seminal vesicle. The posterior wall of the bladder was pushed forward by this mass.

FIG. 6.—Emmerich's case. (Zentralbl. f. allg. Path. u. path. Anat., 21, 673, 1910):
View from behind. The urinary bladder occupies the left half of the picture; the left ureter is normal. (The right ureter and kidney were absent in this patient). From the ampulla of the left vas deferens the tumor arises. Both seminal vesicles and the right vas deferens are normal.

Voelcker exposed the tumor by a paracoccygeal approach, severing part of the gluteus muscle, the tuberosacral ligament and the levator ani. After incision of the visceral pelvic fascia the rectum was pushed towards the midline and the smooth surface of the tumor came into view. Most of the tumor was shelled out; a small portion which was adherent to the bladder had to be left behind. The patient was discharged after three weeks. When seen six months later he was in perfect health.

The specimen was a fist-sized tumor which, grossly and microscopically, looked like an ordinary myoma. It contained a small cavity without epithelial

lining. Voelcker explained the tumor as a myoma originating from remnants of the müllerian duct. No illustration is given.

In the same year (1912) Ceelen described a huge "Fibromyoma of Seminal Vesicle." It was found, protruding retroperitoneally from the small pelvis, at the autopsy of a 67-year-old man who had died of cirrhosis of the liver. No mention is made of clinical symptoms. The tumor had the size of a baby's head; rectum and lower sigmoid were pressed against the sacrum. The thick-walled urinary bladder was pushed to the left and pressed against the anterior aspect of the tumor. The prostatic portion of the urethra was drawn out, the prostate, which was not hypertrophic, was elongated, with its posterior surface firmly pressed against the tumor. Both ureters were

FIG. 7.—Voelcker. (Chirurgie der Samenblasen, 1912): Remnants of midportion of right müllerian duct. The genital tract is filled with collargol. Metal probes are inserted into the ureters.

compressed, their upper portions were as thick as a pencil. The right kidney was normal, the left kidney pelvis was distended, and the kidney substance only 1 cm. thick. The bladder mucosa was trabeculated, the ureteral openings could be probed easily. The colliculus was distinct. The right ejaculatory duct was missing, there were two lumina on the left side. The left seminal vesicle and vas deferens were normal. The right seminal vesicle, which appeared much smaller, was continuous with the tumor, the right vas was stretched over the tumor. The center of the mass was formed by a cavity with shaggy, partly necrotic wall; it contained dull grayish-red fluid with blood clots. The outer solid portion was 3–4 cm. thick, yellowish-gray and

grayish-white. The histologic picture was that of fibromyoma; some of the muscle cells contained pigment similar to that found normally in the muscle of the seminal vesicle. No illustration is given; and nothing is mentioned about histogenesis.

After a long interval (1930) a fourth case was reported, by Panà, under the title "Leiomyoma of Seminal Vesicle and Ductus Deferens, on the Basis of Malformation." This tumor also was found at autopsy. The 59-year-old man had suffered from tabes, syphilitic aortitis and chronic kidney disease. A pear-shaped retroperitoneal mass (8 x 7 x 5 cm., weighing 110 Gm.) was attached to the left seminal vesicle by means of a hollow pedicle, 9 cm. long, 1.5 cm. thick. The lumen of the pedicle was continuous with that of the seminal vesicle and with an epithelium-lined cavity in the pear-shaped mass. This cavity was lined with cuboidal epithelium; there were neither glands nor pigment. The gross and microscopic picture was that of myoma. There was a moderate right hydronephrosis caused by compression of the ureter. Panà interprets the pedicle as either left ampulla or hypoplastic left seminal vesicle. He considers the possibility of a müllerian remnant with hypertrophy of muscle.

Somewhat similar to these cases, but only as large as a cherry, was a cyst Luksch found at autopsy, in 1903, between the vasa deferentia of a 54-year-old man. The wall consisted of smooth muscle, the cavity was lined with a single layer of epithelial cells. Luksch considered it as müllerian.

COMMENT.—Large tumors in the female pelvis frequently are symptomless (myoma uteri, ovarian cystoma), because they may have grown slowly and need not interfere with important functions. The situation is the same with these tumors of the seminal vesicle or ampulla; thus, the fact that most of these tumors have been found accidentally is not so astonishing.

In Voelcker's case only, clinical symptoms (pelvic pain) were present. They appeared in the fourth decade, 15 years before operation. One may assume that the slowly growing myomatous tumor had then existed for some time previously. The three other tumors reported in the literature were found at autopsy of old men (74, 67 and 59 years). There is no way of knowing at what time of life they may have formed or had attained their final size. The same applies to our case, in which the detection of the tumor was hardly less accidental. One might point out the fact that these tumors, while based on malformation, became manifest late in life; but it would be futile to speculate about the causes of this seeming discrepancy.

These tumors resemble myoma uteri so closely that the idea of müllerian origin will present itself almost automatically. Emmerich speaks only about congenital malformation, not mentioning müllerian origin specifically; there is hardly any doubt in our mind that Emmerich's tumor is müllerian, in spite of Schneider's attempt at tracing it to ureteral muscle.

Voelcker, as mentioned, considered his tumor as a myoma originating from remnants of the müllerian duct. In his monograph on the surgery of the seminal vesicles Voelcker shows a beautiful roentgenogram of a müllerian

remnant in a 58-year-old man (Fig. 7). He feels that by filling specimens with contrast substance one might find more of these very rare malformations.

Ceelen gives no opinion concerning the genesis of his "Fibromyoma of Seminal Vesicle."

Luksch mentions the müllerian nature of the cyst, and Voelcker agrees with him.

Some of the smaller cysts of seminal vesicles (Schwarzwald) and some of the retrovesicular cysts, as mentioned by Priesel, are also explained as remnants of the midportion of the müllerian duct. The remnant of the proximal portion of the müllerian duct, the hydatid of Morgagni, is an almost regular finding; the remnant of the distal portion, the utriculus, belongs to normal anatomy, but the midportion usually disappears early in embryonic life, without leaving traces. Vestiges of it have been described (Priesel, Voelcker, Luksch). They are considered great rarities, and it is even more uncommon that they develop into a tumor, as in our case. It remains unknown under what exceptional conditions this happens.

There is no preference for the right or left side. The right kidney and ureter were absent in Emmerich's case. In Ceelen's case the right ejaculatory duct was missing, while two lumina were found on the left side. Panà's case showed no further malformations, neither did Voelcker's, nor did ours (as far as this can be determined in the living patient).

The tumor in our patient obviously originated from the point where ampulla and seminal vesicle meet.

SUMMARY

A large myomatous tumor, closely resembling uterine myoma, has been found attached to the ampulla or seminal vesicle of a 66-year-old man.

Remnants of the midportion of the müllerian duct are the source of these tumors.

Only four such cases have been reported, one of them in a living patient.

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TERATOMA OF THE TESTICLE*

METASTASIS TO THE EPIGASTRIUM TREATED BY BILATERAL ORCHIDECTOMY—RECOVERY

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BY ANIMAL EXPERIMENTS Huggins, and his coworkers, found that androgens stimulated prostatic secretions and that estrogens put an end to the flow of this substance. With stimulations by the androgens the epithelial cells of the prostate became hyperplastic and metaplastic. The hyperplasia was so marked as to resemble cancer. Following treatment with estrogens they promptly returned to normal. After further study and observation Huggins began to castrate men for metastatic cancers of the prostate, with brilliant results.

In June, 1942, Doctor McClelland before the American Urologic Association meeting in New York, in discussing one of the speaker's papers, reported a patient who had embryonal carcinoma of the testicle, with generalized metastases and after removal of the normal testicle the patient improved, with general disappearance of all the metastases, as evidenced by palpation and roentgenograms of the epigastrium and the lungs.

The patient was a Norwegian flier, age 26, who had embryonal carcinoma of the testicle. This testicle was removed in April, 1941. In September, 1941, roentgenograms showed metastases in the lungs, and in October, 1941, a palpable tumor mass appeared in the epigastrium. He was losing ground fast. Thinking that this might be a genital tract tumor influenced by testicular secretions, as in carcinoma of the prostate, and having Huggins' work in mind, it was decided to remove the other testicle. This was done. Two months later the epigastric mass could not be palpated, and three months after castration there was no roentgenologic evidence of metastases. The patient gradually improved, and when last seen in May, 1942, he was to resume his flying. No roentgenotherapy was given after the second operation, although he had three courses of high voltage roentgen-ray treatments prior to October, 1941.

Doctor McClelland reported another case who had teratoma with lung mestastases. The patient did well after removal of the second testicle in February, 1942. However, the condition was too far advanced, and he received some roentgen-ray treatments. Death in this case occurred in July, 1942.

After hearing about these amazing and extraordinary results, I decided to employ bilateral orchidectomy upon a patient of mine whom I was called

*Read before the Philadelphia Academy of Surgery, November 1, 1943.

to see in August 24, 1942, and who was admitted to the Jefferson Hospital August 27, 1942. It took a lot of courage for the patient to consent for the removal of the normal testicle. He consented with the full knowledge that he would lose the power for sexual intercourse. As to propagation, his wife had had a pelvic operation and could not have any children. The wife, being advised about the operation, and fully understanding the consequences, agreed to the operative procedure.

Case Report.—J. L. B., white, male, age 50, complained chiefly of loss of weight of 53 pounds in six months; pain in the left testicle and the left groin, with radiation down the thigh; swelling of the left lower extremity; chills and night sweats.

Previous History.—In 1916, while playing baseball a batted ball hit his testes, at which time he felt some sharp pain for a few minutes. He did not stop playing, and no trouble, such as swelling or discoloration of the scrotal sac, was noted. In 1938, while on a ship, the left testicle became swollen and painful. This condition lasted for about two months, and the only treatment which he received was local application of some ointment. He had had no other illness, and always enjoyed good health.

Present History.—In December, 1941, he began to feel some discomfort in the left testicle and occasional pain in the groin. This gradually grew worse, and later he noticed some swelling and redness of the scrotum, and swelling of the left lower extremity. He also began to tire easily, accompanied with pain in the back when walking. There was an appreciable loss of weight, from 186 to 133 pounds. He never vomited or spat blood, and no blood was noted in the stools. He had received no medical aid until first examined by me August 24, 1942.

Physical Examination.—The patient was an emaciated and undernourished individual, with marked pallor and sallow complexion, who was very nervous, irritable, and toxic. Pulse 110, respirations 20, temperature 101° F. There was a nonpulsating visible mass in the epigastrium which did not move with respiration; the scrotal sac was large and swollen, and somewhat reddened; the left lower extremity was twice the size of the right one; and the venous circulation was more prominent on the left side as compared to the right.

There were no enlarged cervical or supraclavicular nodes. The mass in the abdomen occupied the whole epigastric region. It was about eight inches in diameter, well circumscribed, smooth, nonfluctuating, and its movability was limited. The inguinal nodes were palpable, but there was little variation on the two sides. The left testicle was not tender, however, it was two and one-half times the size of the right one, and was smooth and firm in consistency. The left lower extremity showed no tenderness on pressure and no pitting edema. Pulsation was present in the femoral arteries. Rectal examination was negative. *Provisional Clinical Diagnosis:* Carcinoma of the testicle, with metastases.

On August 25, 1942, a roentgenogram showed a large tumor mass just to the left of the spine in the lower dorsal and upper lumbar region. There were several areas of calcification within the tumor. The psoas line was obliterated. A barium meal showed a normal esophagus, stomach, and duodenum. Roentgenograms of the chest showed no abnormality in the lungs or heart. None of the roentgenograms showed metastases to the bones of the spine, pelvis, hip joints, or the ribs. *Roentgenologic Diagnosis:* Metastatic retroperitoneal mass.

Laboratory Data: Blood Wassermann negative; urine negative; hemoglobin, 55 per cent; R.B.C. 3,200,000; W.B.C. 8,600, normal differential. The patient received a transfusion of 500 cc. of blood.

Operation.—September 11, 1942: Under local anesthesia, a bilateral orchidectomy

was performed, at the same time resecting the spermatic cords as high as possible. The operative recovery was uneventful. After receiving two more blood transfusions, the patient was discharged from the hospital September 23, 1942.

Pathologic Examination.—In the parenchyma of the left testicle there was a yellowish body, 2 cm. in diameter, with a whorl-like formation. Histologically, the hematoxylin and eosin stained section showed a division of the tumor into a number of alveoli by the fibrous tissue. The cells were quite large, arranged in sheets, and had a clear cytoplasm with round and oval nuclei. There were many hyperchromatic nuclei and few mitoses. The tissue was vascular and showed extensive necrosis. The right testicle presented no pathologic changes. *Pathologic Diagnosis:* Teratoma of left testicle.

Postoperative Course.—The patient received roentgenotherapy over the epigastric mass and from the back over the vertebral column. Roentgenotherapy was employed mainly to reduce the size of the large tumor mass, as it interfered with the lymphatic and blood circulation by pressure on the vessels and probably blockage of the lumens with metastatic deposits. This mechanical obstruction produced the enormous increase in the size of the left lower extremity.

These treatments were given in fractionated doses from August 28 to September 18, for a total of 3,500 r. units. They were stopped because the patient developed a marked leukopenia. The white blood cells decreased from 10,900 on August 28 to 3,300 on September 21. No roentgenotherapy has been employed since that time.

Subsequent Course.—After the operation there was a steady improvement in patient's general physical condition. The tumor mass in the epigastrium gradually disappeared, and finally, by November 1, 1942, could not be palpated. The weight increase was remarkable, increasing from 133 to 148 pounds by October 30, 1942; 185 pounds by March 22, 1943; and 197 pounds by October 27, 1943. The swelling in the left lower extremity slowly subsided, and the elastic bandage which he used on the leg was discarded by February, 1943, when the measurements of both thighs had become the same. A recent blood examination showed R.B.C. 4,200,000; W.B.C. 6,500; hemoglobin 82 per cent. When seen October 27, 1943, the clinical examination was absolutely negative. There was no evidence of recurrence at the site of operation or any other place in the body.

One of the most significant examinations was the uranalysis by the Endocrine Laboratory. On September 3, 1942, the Friedman test was positive on two animals, while the qualitative serum gonadotropins were 330 mouse units per 100 ml. of blood, which is an enormous increase from normal and well within the range of pregnancy. The urine estrogens were within normal as were the 17 ketosteroids. On October 24, the Friedman test was negative, the quantitative serum gonadotropins were nondemonstrable, and the quantitative urine gonadotropins were 56 mouse units for 24 hours. The urine values were slightly high, and the serum values were within normal. About six months later, on February 23, 1943, the serum gonadotropins were 10 mu. per 24 hours, both of which are within normal range. On October 13, 1943, the Friedman test was negative, and the urine gonadotropins were 20 mu. for 24 hours, which is also within the normal range.

It is well known that an increase in the gonadotropins is indicative of hyperactivity in the chorionic tissue either in the primary focus or in the metastases. In this patient these tests are very important, because, so far, they show there is no functionally active chorionic tissue. I believe these kinds of hormone assays and tests are very essential in judging the progress of this type of pathology.

Besides the clinical and the hormone assays, follow-up roentgenologic study was made October 27, 1943. The report was that there is no roent-

genographic evidence of metastases in the lungs, pleura, ribs, spine, or shoulder girdle. The heart was normal. There were no tumor masses in the abdomen, and the kidneys showed normal outline. The psoas lines were normal and no metastases were found in the lumbar spine or the pelvis.

Another interesting observation was that the patient reported he had a penile erection, February 1, 1943, which lasted for one minute, and another on February 6 which lasted for a longer time. On March 19, the patient had an erection which lasted for five minutes, at which time he attempted sexual intercourse, but his wife was not responsive. Since that time he has often had slight erections which last only for a few minutes.

SUMMARY AND CONCLUSION

A report is made of a patient who had a teratoma of the left testicle, with a large metastatic retroperitoneal mass. He was treated by bilateral orchidectomy, which was supplemented by the use of roentgenotherapy to reduce the epigastric mass. Fourteen months after the operation the patient is enjoying the best of health. On physical examination October 27, 1943, including hormone assays and roentgenologic studies, he showed no evidences of tumor recurrence.

It is not known what relation there is between sex hormone and cancer, but apparently there is some carcinogenic agent which must have been influenced by the removal of the testes. I realize it is too early to draw any conclusions, however, this report is made with the hope that others might apply the same procedure and record their results. It will be very gratifying if their patients benefit as much as mine has up to the present time.

COMPOUND FRACTURE OF THE FINGERS

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A METHOD is herein described for the treatment of compound fractures of the fingers which has enabled the author to obtain better results, with reduced loss of working time and cost of treatment. The method is not original. It is one which Orr[1] and Trueta[2] have applied to compound fractures of the larger bones, adapted to the fingers.

Finger injuries probably outnumber injuries to other parts of the skeletal system. Since fingers are in a sense the tools of the laboring man, finger injuries result in a significant loss of industrial time.

Despite these facts, finger injuries have not received the serious consideration they merit. As late as 1941, Couch[3] and Oldham[4] published what appear to be fundamental principles for finger amputations. The fact that surgeons have not been familiar with these principles for years is an indication of their attitude toward all finger injuries.

With the present emphasis on industrial loss of time, all treatment of laboring persons must be considered from the point of view of loss of working time as well as end-results. Methods of treatment which were satisfactory in peace time may be inadequate in war time because they do not give a good result with the least loss of industrial time.

Costs of treatment are being studied carefully in the present effort to increase industrial efficiency. Poorly devised methods of treatment of finger injuries, loss of working time and poor functional results following finger injuries contribute significantly to the high cost of treatment.

METHOD OF TREATMENT

Compound fractures of the fingers were treated as emergencies to prevent infection. In only one case was shock sufficiently severe to require the administration of 500 cc. of blood plasma.

The majority of the patients were taken to the operating room. The wisdom of this procedure was soon apparent. It was obvious that compound fractures of the fingers, as well as many other types of finger injuries, did not receive adequate care in the hospital dispensary.

General anesthesia, nerve block at the wrist or brachial plexus was employed with satisfaction. Local anesthesia was rarely employed. Compound fractures of the fingers were usually associated with crushing injuries and edematization of the tissue, therefore local anesthesia would have placed a further burden on the tissues or even caused gangrene.

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Mechanical cleansing was the first step in the surgical care of compound fractures of the fingers. The entire hand except the wounds, was scrubbed for ten minutes with a brush, soap and water. When grease was present the scrubbing was preceded by a cleansing with benzene followed by ether. The hand was rinsed with sterile saline solution. The arm was elevated to empty the veins and a tourniquet was applied to the upper arm. The skin of the entire hand was prepared with an antiseptic, and care was taken not to permit any of it to enter the wound. The entire hand was draped with sterile linen. The surgeon, wearing a cap, mask, sterile gown and a pair of sterile gloves, continued the mechanical cleansing. The entire wound was explored. Foreign material was searched for and removed from the depths of the wound. The wound was again cleansed with copious amounts of sterile saline solution.

Careful débridement was the next step. An efficient mechanical cleansing facilitated this procedure. Tissue that had been irreparably damaged was excised. Blood vessels, nerves and tendons were preserved. At times, skin flaps which might have impaired drainage were present and they were removed in part or wholly. When the nail was involved in the injury it was completely removed to allow adequate drainage, to permit thorough cleansing, and to eradicate a source of infection.

After débridement the tourniquet was removed and bleeding vessels were clamped accurately and ligated with No. 80 cotton. The entire wound was frosted lightly with sulfanilamide crystals. The fracture was reduced. The same principles of reduction and maintenance of reduction that apply to simple fractures of the fingers were employed in compound ones.

Rarely was suturing done. Proper splinting with plaster encasements achieved a degree of wound coaptation that could not be improved by sutures which are tied without tension. Furthermore, tight closure of the wound was undesirable.

A small sterile gauze dressing was placed over the wound and the finger bandaged lightly. An unpadded encasement was applied to the finger. Holding it in the desired position the plaster bandage was made to immobilize the joint above and the joint below the fracture; in case of a fracture of the proximal phalanx, plaster was applied to the hand but did not include the uninvolved fingers.

The encasements were heavy enough to maintain reduction and protect the finger from further injury, but were not large and awkward. The most satisfactory encasements were made from the so-called "specialist splints," which are made by Johnson & Johnson. Six layers of these splints were cut to form two sugar-tong-type of splints which were applied in an anteroposterior and a radio-ulnar direction. The splints were molded together to form an encasement. By making the encasement in this manner the danger of a tight plaster bandage such as might be applied by circular turns is avoided.

The hand was elevated for several hours after operation. A prophylactic dose of gas gangrene and tetanus antitoxin was administered after the usual

skin test. If the patient was not sent back to work immediately or the following day, one gram of sulfadiazine was administered every four hours.

The hands were examined daily for three days. The condition of the base of the finger, the regional lymph nodes, and the patient in general, were accepted as evidence of infection in the wound. The encasements were removed after one to two weeks and, if necessary, another plaster bandage was applied at that time.

MATERIAL

There were 37 patients, with 38 compound fractures of the phalanges. All of the patients were laboring men between the ages of 18 and 61.

The type of injury was severe as a rule. In 35 instances the patient suffered a crushing type of injury. One patient caught his fingers in an electric fan. Another patient struck his finger on an emery wheel and, in addition to the compound fracture, much of the soft tissue was abraded.

Table I indicates the finger involved. The compound fractures involved the distal phalanx in 26 instances, the middle in six and the proximal in six.

TABLE I

FINGER INVOLVED

Thumb	6 fractures
Index finger	10 fractures
Third finger	14 fractures
Fourth finger	6 fractures
Fifth finger	2 fractures

The fractures were comminuted in 17 cases, and involved a joint in five instances. There was appreciable displacement in 20 cases.

Sixteen of the 37 patients lost no working time. The loss of working time is given in detail in Table II because it is such an important factor in finger injuries. Hospitalization was required in 11 cases, for a total of 33 days.

The total cost to the insurance company was made available to the author in 26 cases. The average total cost per patient was $93.87. The highest total cost was $379.00. The average medical cost for all the cases was $33.25. The highest medical cost was $77.00. The payment of compensation to the patient and the hospital costs represent the difference between the total and the medical costs.

There were seven amputations. Six were at the distal interphalangeal joint, and one was at the proximal interphalangeal joint. There were four primary amputations. Three secondary amputations were performed because of gangrene, nonunion of a fracture, and a painful amputation stump due to tight flaps at the primary amputation.

There was no clinical evidence of infection in any of the cases. Cultures were not made.

The end-results were considered good when the man returned to his

TABLE II

LOSS OF WORKING TIME

No. of Patients*	No. of Working Days Lost
16	0
1	1
1	2
1	3
2	6
1	10
1	11
1	15
1	18
1	30
2	32
1	34
1	38
1	39
2	40
1	50
1	54
1	188

*One patient changed jobs during his period of disability. Although his exact loss of time is not known, it is certain that he is doing technical work similar to that which he did before injury.

previous work and did it efficiently and without discomfort or hazard due to his injured finger. In every case the end-result was good.

DISCUSSION

The complete absence of infection clinically attests to the efficacy of this type of treatment which has previously proven itself so successful in the treatment of compound fractures of the larger bones. The healthy condition of these wounds is a marked contrast to the condition of finger wounds which have been given inadequate surgical care in a hospital dispensary and not splinted effectively.

The universally good functional results are important. It must be stressed again that these men are laborers and the results are measured functionally and not anatomically. The patients were able to return to their previous work satisfactorily. They had no significant discomfort in their injured fingers. The injured finger was not awkward and did not present an industrial hazard which predisposed to further injury.

The loss of working time can be profitably discussed. The 16 men who lost no days of work represent the best results. Five other patients who lost a total of 12 working days may also be regarded as acceptable results.

One patient had portions of two other fingers previously amputated and although the encasement on the injured finger would have permitted him to work, he was unable to do so satisfactorily because of the previous amputations. Another patient lost 32 days because in addition to his compound fracture he had an avulsion of a part of the fat pad over the palmar surface of the distal phalanx. A pedicle graft from the thenar eminence of the hand was applied.

Two of the earlier cases could have returned to work sooner if a more

carefully applied plaster encasement had been used. One of these men was injured on an emery wheel and had extensive loss of the soft tissues over the palmar surface of the proximal phalanx. These men lost 11 days each.

One patient lost 50 days because poor judgment was used in his initial surgical care and the distal phalanx became necrotic and had to be amputated secondarily. A primary amputation would have saved him at least 35 days. One man lost 10 days because an amputation was undertaken with tight flaps. This was an error in judgment. The insurance company paid him for the loss of the entire finger, and it was later amputated because of discomfort.

Two patients who had sustained severe crushing injuries of their fingers suffered intense pain in the ends of their fingers that suggested minor causalgia. After the wounds were healed, merely touching the fingers with cotton caused marked pain. Injection of the cervical sympathetic nerves or the appropriate peripheral nerve with procaine hydrochloride was not done, but should have been done. In more recent cases the author has had gratifying results from this procedure.

One man lost 188 days. While holding a stake his thumb was struck with a 12-pound sledge hammer. He sustained a compound fracture of the proximal phalanx of his thumb. The fracture was comminuted but the phalanx was split longitudinally into two major fragments. The fracture did not unite. He was given a choice between a bone graft and amputation preserving the viable proximal fragment. He chose the latter and is now working with a good functional result. The decision to perform a secondary amputation was postponed much too long. Probably six weeks would have been sufficient time to allow for callus formation from both major fragments. The decision to intervene would have been easier to make had he been able to work with an encasement on for about three weeks. This was impossible because of severe causalgia-like pain. Nerve block in this case might have saved much lost working time.

An emotional factor contributed to the loss of working time in five cases, who lost a total of 141 days. One man was known as a chronic job changer. He refused to work, whether he could or not, until his wound was healed. Soon after it was healed he quit his job. In one case impending induction into the army was thought to prolong disability. One man was later found to be working elsewhere while he was being paid compensation. In the two remaining cases the patients probably could have been persuaded to return to work.

The industrial surgeon must be alert to his responsibility to return patients to work as soon as they are able. Very often an intelligent discussion with the patient will allay some imaginary fear and result in a much shorter period of disability. At times it is important to call the patient's employer and determine whether there is some type of work which the patient may do despite his disability. The personnel manager of the plant has a responsibility in this procedure. If a man with partial disability is given a job where his associates must do part of his work for him, ill feeling or industrial hazard to

his fellow workmen may result. If light work must be created for the disabled man, the cost may be higher than that of compensation.

Encasements for injured fingers have been extremely successful in the author's experience. They achieve perfect splinting and complete rest for the finger. With the use of encasements all finger nails involved in the injury are completely removed. The plaster bandage provides a better splint than the injured nail and avoids any disability due to the loss of the nail. Furthermore, with the removal of the entire dirty nail a source of infection is eradicated.

Probably the greatest advantage of the encasement is the prevention of further injury. It is this factor which the patients appreciate most for they can work painlessly while the finger is healing. They often volunteer their appreciation for the plaster bandage and frequently ask for another one to be applied when the time to discontinue immobilization comes.

The simple technic of application of encasements to fingers has been described. It is worth emphasizing that the encasements are formed of molded plaster splints, which procedure avoids a tight plaster bandage that might result from its circular application. With a little practice encasements which will give perfect immobilization and protection from further injury, and yet not be awkward, can be made. Plaster encasements are easier and quicker to apply than wooden or metal splints. They are more efficient and more comfortable than such splints. No difficulty with tight encasements or stiffness of fingers due to them has been encountered. They can be removed easily with a heavy pair of bandage scissors. In the early cases men sometimes asked to have plaster bandages removed because they were dirty. Covering the encasements with cotton or leather stalls while working solved this problem.

The use of encasements on injured fingers is part of the infrequent dressing technic. The dressings are done at intervals of one to two weeks. This procedure saves time, money and discomfort to the patient. It prevents secondary wound infection.

It is very gratifying to the patient and doctor to see the healthy or healed wounds when the encasements are removed. It is obvious at this time that sutures (tied without tension) would not have resulted in better wound coaptation than the encasements afforded. Furthermore, sutures would tend to act as foreign bodies and impede drainage.

In addition to compound fractures, encasements have been applied frequently for simple lacerations and infections of the fingers. In such cases they have been very successful and have been the deciding factor between the man working and not working. Lacerated fingers are rarely sutured because here, too, encasements have afforded as good skin coaptation as sutures.

The question of amputation often arose. Discussion of all the factors involved in finger amputations does not lie within the scope of this paper. Any surgeon treating finger injuries must be familiar with the intricacies of amputation, including the proper levels for the various fingers and the technical points which will result in a painless, useful stump. The reader is referred to the excellent articles by Couch[3] and Oldham[4] on finger amputations.

In finger amputations, the old maxim, "save all you can," is not tenable for the results in working men are measured functionally and not anatomically. If an amputation is not performed when one is clearly indicated, the wound may heal kindly but the patient will have a finger which is an industrial hazard and a cause of suffering or further injury to him. The insurance company will pay him for the loss of such a finger and to be rid of his disability he will have it amputated later. Such a complication increases the loss of working time and the cost of treatment.

Crush injuries of the distal phalanx are often amputated because of the fear of gangrene. With the closed-plaster technic, surprisingly few are not viable and do not give a good functional result.

A logical criticism of this report might be that 26 of the 38 compound fractures involved the distal phalanx and since loss of this phalanx results in no handicap to the patient,[5] all these fractures might better have been treated by primary amputation. Usually, however, the crush type of injury which caused these compound fractures did not leave sufficient soft tissues for satisfactory flaps for disarticulation at the distal interphalangeal joint, and an amputation higher than this joint would have been necessary to avoid tight flaps and secondary amputation. Even if some of the cases had had a satisfactory disarticulation at the distal interphalangeal joint, it is doubtful if their loss of working time would have been shortened and the results would not have been better since in all the reported cases the functional results were good.

Compound fractures of two phalanges with shattering of the joint between them yield poor functional results and primary amputation should be undertaken.

It is often recommended that compound fractures of the fingers associated with a severed tendon be subjected to primary amputation. This is not always true. The author had one such case which was not amputated and a good functional result was obtained. This patient does skilled labor.

The cost of finger injuries is not insignificant. An average total cost of $93.87, and an average medical cost of $33.25 represent sizable amounts when the total number of cases is considered. A survey made by the author at one plant, for the year 1942, showed finger injuries to represent 19 per cent of all injuries, and to be the most costly group. If the industrial surgeon is to discharge his duty he must be alert to methods of treatment which will give a good end-result, with a minimum loss of working time and cost of treatment.

A note about sulfanilamide sensitivity is worthy of mention. Sensitivity should be suspected when the wound weeps a thin, serous drainage in copious amounts. Recently I had a simple laceration that showed such a discharge. The encasement became saturated and had to be changed. My first impression was that a serious infection was developing. Consultation with a dermatologist led to the discovery of the true condition, and when sulfanilamide was omitted, the wound healed promptly.

CONCLUSIONS

1. When compound fractures of the fingers receive the same painstaking care which similar fractures of the larger bones do, the results are good. The so-called closed-plaster method of treatment was successfully applied to compound fractures of the fingers. The technic was described.

2. Loss of working time is an important national problem in the present war. Finger injuries account for a significant loss of working time among laboring men. It is the traumatic surgeon's duty to employ forms of treatment which, in addition to giving a good final result, will result in the least industrial loss of time. The closed-plaster technic is such a form of treatment. The encasements assure the fingers complete rest and protect them from further injury. The working men like the encasements because they can return to work with no discomfort long before the wound is healed. Of the 37 patients reported, 16 lost no working time. In the remaining cases the loss of working time was analyzed to determine how it might have been reduced.

3. Finger injuries are expensive, especially when their frequency is considered. In the present series the average total cost per case was $93.87, and the average medical cost per case was $33.25. Surgeons must be attentive to compensation costs, for they are reflected in manufacturing costs. The closed-plaster technic for compound fractures of the fingers is less costly than other methods of treatment, as the men return to work earlier and dressings are done less infrequently.

4. The results of the closed-plaster method of treatment in 38 compound fractures of the fingers were good. In no case was there clinical evidence of infection. In every case the functional result was such that the man was able to return to his previous work and do it efficiently and without discomfort or hazard due to his injured finger.

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REGIONAL ENTERITIS INVOLVING MECKEL'S DIVERTICULUM

PERFORATION OF THE DIVERTICULUM AND FISTULA FORMATION

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REGIONAL ENTERITIS has a predilection for the terminal ileum, as Crohn, Ginzburg and Oppenheimer[1] pointed out in their original description of the disease. Other reports of nonspecific granulomas of the intestinal tract, however, indicate that the same pathologic process may involve any segment of the bowel from the duodenum (Gottlieb and Alpert[2]) to the sigmoid (Dalziel[3]). Furthermore, Ravdin and Rhoads[4] have pointed out the similarity of fibroplastic appendicitis to this process. Meckel's diverticulum only once (Barrington and Norrish[5]) has been a site of the disease and never before has been the point of fistula formation in regional enteritis. For this reason it seemed of interest to record the following case.

Case Report.—Hosp. No. 55860: E. C., white, female, age 23, married. The patient had experienced pain in the right lower quadrant of the abdomen at intervals since the birth of her first child three years ago. The pain was accompanied by tenderness and the attacks usually lasted from one to three days. They increased in frequency and severity until three months before admission. It was decided that celiotomy be performed. This was carried out July 10, 1943, at the Good Samaritan Hospital, Lebanon, Pa., through the lower right rectus incision. A large mass was found involving the cecum, terminal ileum, right tube and ovary, all of which were densely adherent to each other. There was marked induration of the mesentery. The tube on the right side was inflamed and the ovary was the seat of a large chocolate-colored cyst. The tube, ovary and appendix were removed. Sulfanilamide was placed in the wound, and Penrose drains introduced.

Following this procedure the patient recovered satisfactorily, but continued to drain purulent material. She was referred to the Hospital of the University of Pennsylvania by her physician, Dr. Clyde Saylor, and admitted on September 25, 1943. The past and family histories were noncontributory. She was a housewife.

Physical Examination.—The patient, a well-developed and well-nourished woman of 23, who was rather pale. Temperature, 98.4° F., pulse, 87, respirations 16, blood pressure, 104/68. Examination was essentially negative except for the abdomen. There was a five-inch right rectus incision with a drainage tract near the midpoint discharging small amounts of creamy pus. At the level of the umbilicus there was a vague rounded mass on the right side. This area was moderately tender. Peristalsis was normal.

Laboratory Data.—Hemoglobin 78 per cent. Leukocyte count 7,200. Flat film of abdomen: Negative. Barium enema: Uncertain, in that it was thought that part of the cecum failed to fill.

Preoperative Diagnosis: Infected mesenteric cyst. The patient was given three grams of sulfadiazine in preparation for operation.

Operation.—September 28, 1943: Under continuous spinal anesthesia, the old wound was reopened and extended upward. Here the peritoneum was entered. Two adherent

loops of small bowel were dissected free from the anterior abdominal wall. Between them a Meckel's diverticulum was found which was adherent to the mesentery. It was freed and found to have a perforation at its tip. It was rapidly removed and the ileum closed. Further exploration then showed that the cecum and terminal ileum were inflamed and thickened and were matted down against the pelvic brim. They were mobilized as was the remainder of the right side of the colon. About two feet of small bowel and the right half of the colon were resected. A side-to-side anastomosis of the transverse colon and the ileum was made.

Pathologic Examination.—The gross specimen consisted of a segment of large and small intestine and the separately excised diverticulum. The intestinal segment included 59 cm. of the terminal ileum, the cecum and approximately 10 cm. of the ascending colon.

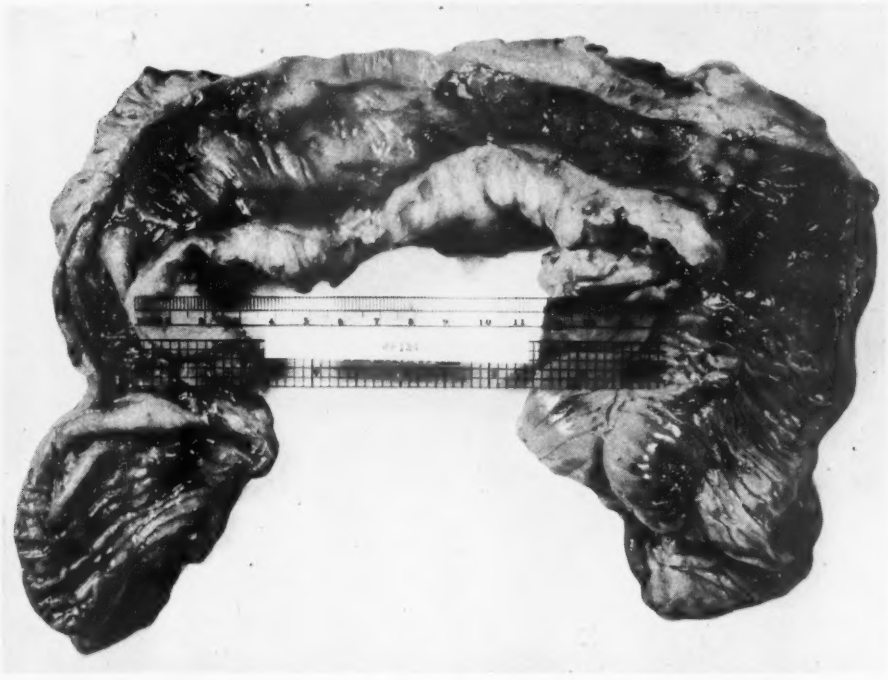

FIG. 1.—Regional enteritis of terminal ileum, cecum and ascending colon. The photograph does not include the proximal half of the resected small intestine.

The appendix had been removed previously. The wall of the distal part of the ileum, especially the muscularis, was rigid and greatly thickened. This produced a considerable degree of stenosis in the terminal 8 cm. The mucosal surface was diffusely reddened and granular, and the folds were either thickened or lost. Usually extending longitudinally along the mesenteric border were a number of superficial, more or less rectangular ulcers. Their edges were irregular and frequently overhanging and their craters were filled with mucoid material. The largest ulcer was 4 cm. long and 0.6 cm. wide. These pathologic changes were marked only in the distal 20 cm. of the ileum, but they extended in diminishing intensity and patchy distribution, proximally for about another 20 cm. The ileocecal valve was strikingly thick and rigid, and a few tiny ulcers were present on its cecal aspect. A small portion of the adjacent large intestine was also involved (Fig. 1). The site of excision of the diverticulum was found 40 cm. from the ileocecal valve, at about the proximal limit of evident disease. The ileal mesentery was thickened and contained a number of enlarged, soft lymph nodes.

The diverticulum was conical, measuring 1.5 cm. in diameter at its base and 3 cm. in length. Its wall resembled that of the less intensely involved portions of the ileum. The perforation at its tip was 2 to 3 Mm. in diameter, and the edges were red, granular, and somewhat indurated. Scarring was not extensive and there was no ulcer crater, except for the perforation itself.

In addition to hyperemia, muscular hypertrophy, and ulceration, microscopic examination revealed considerable degrees of fibrosis and cellular infiltration, most marked

FIG. 2.—Photomicrograph of terminal ileum showing submucosal fibrosis and an inflammatory cell infiltration which extends into the mucosa and the muscularis. The edge of a superficial ulcer is at the right. (× 24)

in the submucosa and somewhat less so in the subserosa (Fig. 2). The inflammatory cells were of varied type, neutrophil leukocytes predominating in the areas of ulceration, lymphocytes, plasma cells, and larger mononuclear cells predominating elsewhere. Large lymphoid follicles were numerous. Occasional giant cells were seen but neither these nor pseudotubercles were a conspicuous feature. The histopathologic changes were of

the same nature in all the parts of the intestine involved, although they varied in degree. In general, they were less intense in the diverticulum (Fig. 3), the cecum, and the proximal part of the small intestine, than in the terminal ileum. This is particularly true with regard to the fibrosis. The mucous membrane of the diverticulum was of the small intestinal type. No heterotopic tissue was found in numerous sections. The perforation was lined by granulation tissue containing many neutrophil leukocytes as well as mononuclear cells, but scarring was not extensive. The lymph nodes showed a nonspecific hyperplasia.

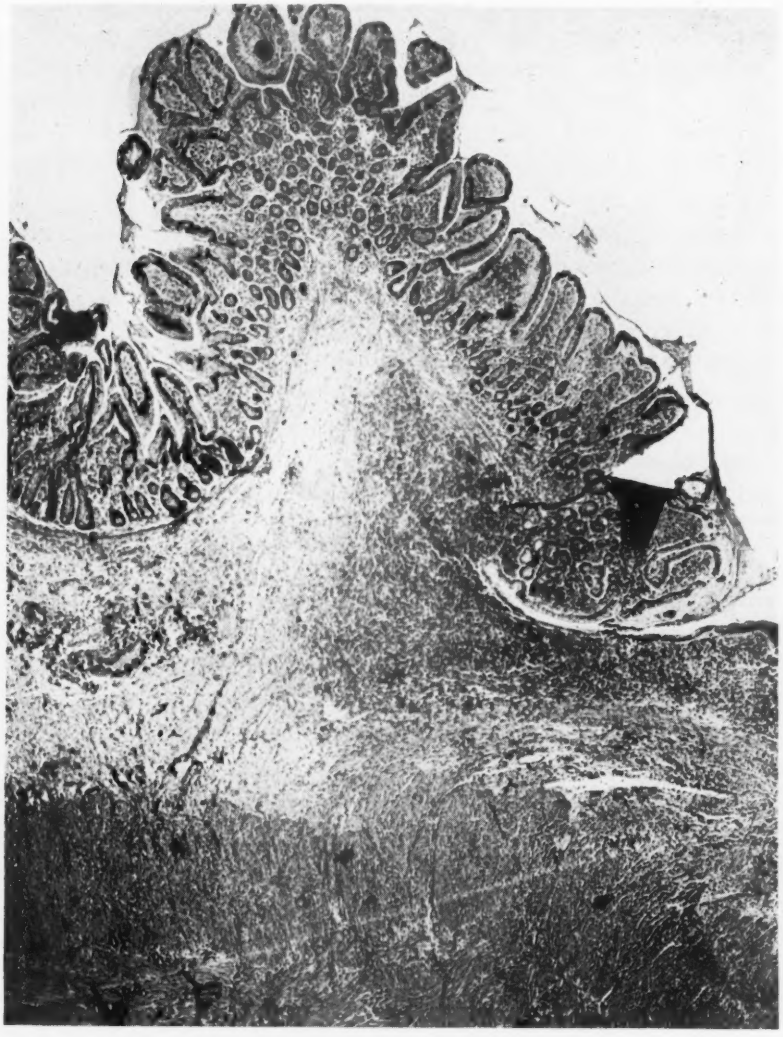

FIG. 3.—Photomicrograph of Meckel's diverticulum showing intestinal type of mucous membrane and a nonspecific, chronic inflammatory reaction. This section was taken from an area adjacent to the perforation. (×32)

COMMENT.—Much has been written about the pathologic changes that may occur in association with Meckel's diverticulum. Perforation is not an unusual event, occurring as a sequela to ulcer or acute diverticulitis with gangrene. The ulcers found in Meckel's diverticula are usually regarded

as peptic (Greenwald and Steiner[6]), although Winkelbauer[7] believes them to be caused by spasm of the diverticula. They may be situated either in intestinal or gastric mucous membrane but in the great majority of cases in which microscopic examination was carried out, heterotopic gastric mucosa has also been demonstrated to be present (Schullinger and Stout[8]). In our case heterotopic tissue was not found after careful study of numerous sections of the diverticulum. Nor did the gross or microscopic appearance of the perforation suggest a similarity to the usual chronic ulcer of the stomach or duodenum. The mucosal linings of the majority of Meckel's diverticula are of the intestinal type, heterotopic tissue being found in only 15 to 25 per cent (Greenblatt, Pund, and Chaney[9]). The possibility that the diverticulum in our case was acutely inflamed at the time of the first celiotomy cannot, of course, be completely ruled out, but the pathologic changes in the diverticulum are entirely similar to those in the ileum, differing only in degree. They do not suggest the previous occurrence of acute diverticulitis and gangrene; nor does the clinical history. Furthermore, the pathologic examination indicates that the disease in the terminal ileum was more advanced than that in the diverticulum and the more proximal part of the small intestine. This sequence of events—inception of the disease in the terminal ileum with progression proximally, perforation, and following appendicectomy, fistula formation—as well as the gross and microscopic appearance of the lesion, corresponds closely to the original description of Crohn, Ginzburg and Oppenheimer,[1] which has since been confirmed by others.[10]

SUMMARY

A case of nonspecific regional enteritis involving Meckel's diverticulum is reported. A fistula had developed following a previous appendicectomy and right salpingo-oophorectomy, and a perforation was found in the diverticulum. The patient recovered following a resection and anastomosis.

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BRIEF COMMUNICATIONS

A PARAUMBILICAL ABDOMINAL WALL CYST*

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THE FINDING of an unusual cyst in the abdominal wall of a patient prompted an investigation to determine its true nature and etiology, if possible. Certain data have been obtained which make the case of special interest.

Case Report.—G. R., colored, female, age 47, entered the Barnard Free Skin and Cancer Hospital, January 14, 1943. For seven or eight years she had known that she had a uterine tumor. This had not disturbed her until one year before admission. It had then begun to grow quite rapidly and subsequently produced a protuberance in her abdominal wall. The gravid appearance rather than pressure symptoms from the growth motivated the patient to ask for its surgical removal.

The patient reported her past health as having been good. She had received therapy for syphilis. She had never been operated upon.

The menstrual history was interesting in the light of later findings. Her periods were always regular and had been 28 days apart since menarche at age 13. Her last menstruation had been three weeks prior to admission. She had experienced neither menorrhagia nor metrorrhagia. The patient had been pregnant seven times—having had four miscarriages and three term births.

Physical Examination.—The patient was an alert, well-developed and well-nourished colored female. The examination revealed as significant data: A saddle nose; a blood pressure of 158/90; a definitely enlarged abdomen which contained a firm, movable mass at the level of the umbilicus; a liver edge which could be palpated three finger's breadth below the right costal margin; and a uterus, definitely enlarged and irregular in outline, which was obviously connected with the abdominal mass. The laboratory examinations revealed no abnormalities. The Kahn test was negative. *Preoperative Diagnosis:* Pedunculated fibromyomata uteri.

Operation.—January 16, 1943: An abdominal hysterectomy was performed under spinal anesthesia (pontocaine, 20 mg.). While extending the lower midline incision to the left of and superior to the umbilicus, a cystic structure was exposed in the subcutaneous layer of the abdominal wall. This was not given careful consideration until the abdominal wall was being closed.

Numerous large, pedunculated masses filled the abdominal cavity. These were connected to a stalk which was attached to the uterine fundus. (One of these had obviously been mistaken for the liver, as this organ could not be seen until after the mass had been displaced anteriorly). After cutting several thick, fibrous adhesions which anchored two of the masses to the posterior abdominal wall, the entire specimen was delivered through the wound. At this point the patient's blood pressure fell markedly. It was necessary to administer supportive measures (intravenous fluids and stimulants) which were effective. A hurried supracervical-type of hysterectomy was performed—the right adnexa being taken while the left were allowed to remain.

During the closure of the abdominal wall, the cystic mass was excised. It was situated approximately one inch superior to the umbilicus and was immediately superficial to the linea alba.

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Gross Pathology.—The intra-abdominal specimen weighed eight pounds. It consisted of the uterus, the right tube and ovary, and the bulky pedunculated fibromyomatous masses, which were attached to the fundus of the uterus by a relatively narrow pedicle. The uterus proper was about twice normal size. Submucous, intramural and subserous masses distorted its shape and all but obliterated its cavity. Several moderately-sized serous cysts were attached to the stalk. Numerous white shreds were scattered over the surface of several of the tumors. Close inspection revealed that these were made up of minute spherical masses not unlike "fish roe" in appearance.

The abdominal wall specimen measured 1.5 x 2 x 3 cm. It had the appearance of a cyst, being of grey color with purple mottling. When the specimen was bisected, it was found to be a two-chambered structure (Fig. 1). A smaller cavity was situated within a larger one. They shared one wall in common. The arrangement was that of a "cyst within a cyst." The outer space contained small homogeneous white ovoid bodies, which were attached to one another. They were considerably larger but otherwise quite similar to the "fish roe" strands seen on the surface of the abdominal tumors. The smaller space contained a thick brown fluid.

Microscopic examination of the sections taken from the uterine masses revealed nothing more than the fibromuscular stroma so characteristic of fibroid tumors of the uterus. The fibrous tissue elements predominated.

A sufficient number of the white shreds were collected from the surfaces of the abdominal masses to embed and make a block for microscopic study. The microscopic appearance of the preparations made from this was that of a homogeneous pink-staining ground substance through which were scattered a moderate number of basic-staining nuclei. A single layer of flattened cells formed a covering for each of the many irregularly-shaped masses composing the section.

The wall of the abdominal wall cyst is made up of fibrous connective tissue. It varies in thickness, being relatively thick where the two cavities have a common wall but being much thinner elsewhere. Fibro-areolar tissue and a small amount of fat is to be found in some areas. The thickest portion of the wall is fairly well vascularized. Exterior to the single layer of fibroblastic cells, which form the lining of the larger space, is a shallow zone of elastic fibers. The contents of this cavity are composed of irregularly-shaped masses of homogeneous pink-staining material having a waxy texture. The microcopic appearance of these bodies is identical with that of the material collected from the surfaces of the fibromyomata.

The small cavity has a wall similar to the large one. The finding of a lining epithelium sets it apart from the outer one. In some areas the epithelium is seen to be cuboidal in type, but generally speaking, it is composed of pseudostratified ciliated columnar cells (Figs. 2 and 3). The basement membrane is smooth for the most part, but the epithelium is raised into papillary folds in a few places.

DISCUSSION.—The proximity of an abdominal wall cyst to the umbilicus suggests the possibility of its origin from a vestigial remnant. Cullen,[1] in his authoritative treatise, does not describe a similar structure as being superior to the umbilicus and superficial to the anterior sheath of the rectus abdominis muscles.

If the patient had previously had an abdominal operation, one could surmise that a fimbria of an oviduct had accidentally been transferred to the abdominal wall. Since she had had no operation, this precluded such a speculation.

There is not any possibility of the cyst being metastatic from the intra-abdominal tumors nor a direct extension from them. The histopathology of

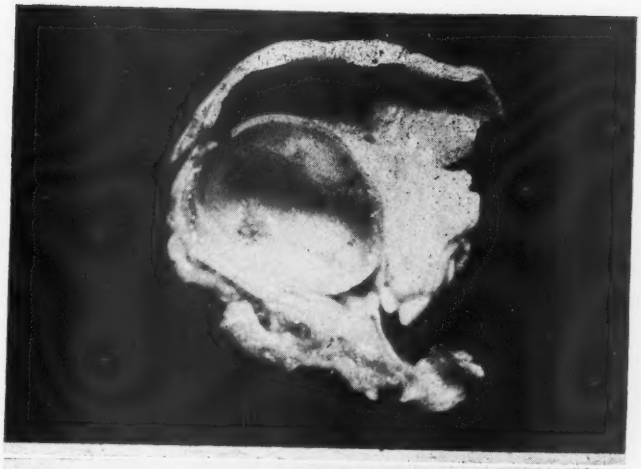

FIG. 1.—The inner, epithelium-lined, cavity of the abdominal wall cyst is clearly seen in the photograph of the bisected specimen. The small, white inclusions of the outer cavity appear rather indistinctly in the upper right part of the photograph. (Approximately actual size)

FIG. 1

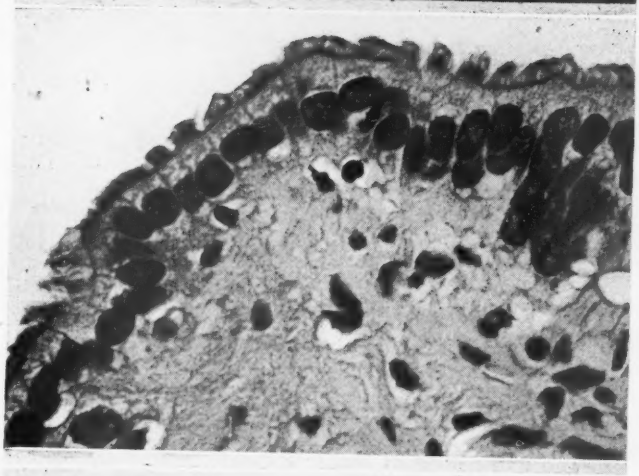

FIG. 2.—A low power photomicrograph reveals the transition from low columnar to the pseudostratified columnar type of ciliated epithelium.

FIG. 2

FIG. 3.—A high power photomicrograph affords a more detailed view of the epithelium showing individual cilia.

FIG. 3

the cyst precludes its direct or indirect relationship with the intra-abdominal fibroids.

A detailed study of the lining epithelium was made in the hope that it might be of help in drawing conclusions. Pseudostratified ciliated columnar epithelial cells normally occur only in the respiratory tract and the genito-urinary system. Dr. E. V. Cowdry was kind enough to study these cells with me. He believed them to be true ciliated cells, but suggested that Dr. Alfred M. Lucas be asked to give an opinion in this regard. Doctor Lucas concluded that the cells are ciliated and do not have a striated cuticular border. He found only one basal body on each cilium. This is the situation found in nasal epithelium. The ciliated cells of the fallopian tube have a diplosome-type of basal body. A preparation was stained with hematoxylin and mucicarmine in an effort to determine the presence of mucus secreting cells. None were detected, but this, in itself, does not rule out a similarity to respiratory epithelium.

Dr. George W. Corner, who also kindly reviewed the slides from the embryologic point of view, concluded that, in all probability, the mass represents an atypical differentiation of local origin (teratoma).

Doctor Cullen graciously responded to say that in his belief, the structure most probably was derived from a remnant of the omphalo-mesenteric duct.

These varying opinions preclude a dogmatic statement as to the origin of the cyst. The presence of identical masses, scattered over the surface of the abdominal tumors on the one hand and being contained within the outer cavity of the cyst on the other hand, suggests a possible relationship between the two pathologic processes.

SUMMARY

The case history of a colored female patient is given. An interesting cyst was accidentally found in her abdominal wall (superior to the umbilicus and superficial to the linea alba) while performing an hysterectomy. One may not dogmatize regarding the specific etiology of this cyst. The opinions of authorities are given.

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MULTIPLE ADENOMAS OF THE JEJUNUM

CASE REPORT

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THE FOLLOWING CASE is reported to record the occurrence of multiple adenomas of the jejunum. There was also an associated adenoma of the colon.

Tumors of the small intestine are not common. Somewhat less than 50 per cent are malignant, *i.e.*, lymphoblastoma, carcinoma, and sarcoma, in order of frequency. The benign tumors encountered are adenomas, argentaffin tumors, lipomas, myomas, fibromas, and miscellaneous other rare types. Adenomas are the most common benign tumors and are found more frequently as a single tumor than multiple. Since they arise from the inner bowel layers, they protrude into the bowel lumen and assume a polypoid form of more or less degree, a significant fact in their symptomatology. Their location may be anywhere, but the greatest frequency is in the ileum, second, the duodenum, and third, the jejunum. All reports agree that adenoma of the jejunum is a rare condition.

The association of small bowel adenomas with adenomas of the colon does occur. In multiple polyposis of the colon the adenomas may extend to the lower ileum. However, the association of adenomas of the jejunum and colon is another matter, and I have been able to find only one instance (recorded by Gerwig and Stone, in 1943), of a single jejunal adenoma associated with multiple adenomas of the splenic flexure of the colon.

The clinical course of the patient to be reported has been followed over a period of 11 years, and serves to emphasize the following features:

(1) The obscure nature of the symptoms associated with small bowel tumors. These may suggest gallstone colic, renal colic, peptic ulcer, or even a primary anemia. Intussusception is a common complication. Celiotomy for intestinal obstruction reveals the true diagnosis very often for the first time.

(2) Intussusception in the adult is always secondary to some underlying condition.

Case Report.—A slim, red-headed female, single, age 22, was first seen in August, 1932, with acute right lower quadrant abdominal pain and vomiting. There was a past history of an operation for "telescoped bowel" at age seven. In addition she described peculiar attacks of abdominal pain and vomiting occurring once or twice a year since the age of 17. The present attack was similar to these, but more severe. On abdominal examination, there was some muscle resistance and an ill-defined tender mass in the right lower quadrant. On vaginal examination, there was another distinct mass,

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The views expressed herein are the writer's and are not to be construed as official or reflecting the views of the Navy Department.

the size of an orange, in the left fornix. The temperature was 100° F., and catheterized urine showed albumin and R.B.C. Following an enema the symptoms were relieved and the right-sided abdominal mass disappeared. Intravenous pyelography showed a stone in the right kidney. This was accepted as the cause of her symptoms and the stone removed ten days later. Recovery was uneventful and she left hospital symptom-free. Within a few weeks her old attacks of abdominal pain recurred. These were commonly not much more than "cramps" referred to the umbilicus, and occurred at intervals of days to weeks. Vomiting was unusual. Roentgenologic examination of the G. U. tract and gallbladder were normal, and the urine was clear.

In July, 1933, she developed a much more severe attack than usual and was brought to the hospital. A tender sausage-shaped mass was palpable in the midabdominal region. An enema produced results but no relief. Exploratory celiotomy disclosed an intussusception of the upper jejunum, ten inches in lengtlf, which was readily reduced. On searching for a cause a polypus, the size of a marble, was noted at the site of the intussusception, while above it were several smaller ones, and still higher, and about 12 inches from the duodenal jejunal flexure, a side-to-side anastomosis marked the site of the operation in childhood. Tracing the bowel downward from the intussusception, three or four small polypi were recognized, and finally one, the size of a walnut, was encountered about at the juncture of the jejunum and ileum. Below this there were none. The upper polypus causing the intussusception was removed by simple incision, ligation of the pedicle at its attachment to the mesenteric border, and closure. A similar process was attempted with the large polypus in the lower jejunum but the slipping of a clamp and hematoma formation necessitated resection and end-to-end anastomosis. The smaller polypi were not interfered with, and the abdomen was closed. Recovery was uneventful.

A postoperative (August, 1933) barium meal showed stomach and duodenum normal, the jejunum shortened, widely dilated, and the lumen almost filled by mucous membrane, thrown into deep folds between which only flecks of barium remained. Two ring-like formations were present, which were suggestive of polypi in the lower portion. The ileum appeared normal, and there was no evidence of delay or obstruction at any point.

Attendance at the Clinic during the next four years, 1933–1937, was sporadic. The chief complaints were continuing attacks of crampy abdominal pain and vomiting at intervals of weeks to three or four months; minor episodes of diarrhea, although the bowels were usually regular; occasional blood in stools; and general debility. The weight remained stationary at 107 lbs. Examination was negative except for moderate secondary anemia, and the mass in the left vaginal fornix. Menstruation was regular. Rectal and sigmoidoscopic examinations were negative. She was able to carry on her work in a factory satisfactorily.

In September, 1937, she again developed a severe attack of abdominal pain and vomiting, and was brought to the hospital. Abdominal examination showed a sausage-shaped midabdominal mass. Manipulation was attempted in the hope of external reduction. Considerable decrease in size resulted, but as no reliance could be placed on this, celiotomy was carried out. No intussusception was found. However, about three feet from the duodenojejunal flexure, an 18-inch segment of jejunum was markedly dilated and edematous. Immediately at the upper margin of this area two polypi, the size of marbles, were palpable, and at the lower border one of the same size. The interpretation was that this was the site of an intussusception reduced by the preoperative manipulation. A thorough exploration of the whole G. I. tract was then carried out. The stomach and duodenum were normal, with no evidences of polypi. The first 12 inches of the jejunum was markedly "mushy," as if from redundant mucosa. No actual polypi were recognizable. Immediately below this was the side-to-side anastomosis, performed at age seven. Three feet below the flexure were the two polypi noted above;

and in the 18-inch loop of edematous jejunum, and at its lower margin, was the third polypus. From this point to the lower jejunum were four or five small polypi; and then the site of the end-to-end anastomosis, of 1933, was encountered. Below this the ileum was normal. Following the large bowel downward it was found to be normal to the middle of the transverse colon, where a polypus, the size of a walnut, was found. All

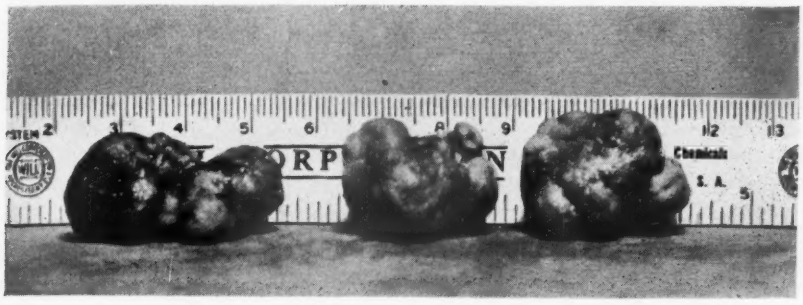

FIG. 1.—Three adenomas removed at 1937 operation.

FIG. 2.—Photomicrograph of adenoma shown in Figure 1.

polypi, including this one, had the characteristic of being attached to the mesenteric border by distinct pedicles. The remaining colon and rectum were entirely normal.

The two polypi above and one below the segment of edematous bowel were removed through small incisions. The other small bowel polypi were not interfered with. When the sigmoid and rectum were palpated for polypi the pelvic tumor was

noted. It was delivered and found to consist of a solid tumor and a cyst, each the size of a small orange, arising from a common pedicle and replacing the left ovary. These were removed. The uterus was noted to be enlarged and smooth. It was felt removal of the colon polypus should not be attempted at this time. The abdomen was closed in layers. Recovery was uneventful.

The subsequent clinical course of the patient was complicated by the fact the ovarian tumor proved to be a malignant granulosa cell tumor of the ovary, which eventually showed evidence of metastases (April, 1941). These, however, responded well to roentgenotherapy, and she is still in fairly good health today. A barium enema, in October, 1937, demonstrated the single polypus in the transverse colon, which was otherwise normal.

As far as the intestinal adenomas were concerned, the patient continued to have attacks of abdominal cramps and vomiting at various intervals, and of varying intensity, but, on the whole, of minor degree. There have been also minor episodes of diarrhea and, at times, gross blood in the stools. There has been a definite tendency to anemia. Removal of the colon polypus was urged from time to time (until the problem of metastatic malignancy from the ovarian tumor arose), but consistently refused.

Probably the diarrhea and gross blood in the stools can be attributed to the colon polypus. The episodes of abdominal pain and vomiting may have been due to either the large or small bowel tumor. There was no consistent association between these two occurrences, *i.e.*, diarrhea, the abdominal pain and vomiting.

The secondary anemia was certainly contributed to by the colon polypus although the small bowel tumors may also have been a factor.

SUMMARY

The clinical course over a period of 11 years of a case of multiple adenomatous polypi of the jejunum, associated with an adenoma (probable) of the colon, has been recorded. Episodes of abdominal pain and vomiting, of varying intensity, were characteristic. The more severe attacks were associated with intussusception and required operation. It is possible that even in minor attacks intussusception of some degree occurred and were relieved by spontaneous reduction. Low-grade secondary anemia was a well-marked feature.

In spite of all these handicaps this patient is alive; enjoys relatively good health; and when last heard from was attempting to enlist in the W. A. C. S.

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FORUM

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Re: **Discussion by Kellogg Speed, M.D. of article by D. E. Robertson, M.D. appearing in** ANNALS OF SURGERY, **118, 318-328, August, 1943.**

ABRAHAM O. WILENSKY, M.D., NEW YORK, N. Y.:

"The discussion on Dr. D. E. Robertson's paper in the August ANNALS OF SURGERY, on Osteomyelitis made by Dr. Kellogg Speed, carries the following statement in reference to the work of Wilson and McKeever; namely, that: 'Together with Wilensky, they still favor operation for established osteomyelitis.' I am rather surprised at this because I have always tried to make it clear that the only two indications for operation which I have ever made were (1) the presence of a frank abscess in the soft parts which is anatomically within surgical reach; and (2) the removal of a sequestrum which is acting as an irritating foreign body. I have always favored leaving the cure of the osteomyelitis to nature except for these two indications."

Rebuttal to the Objections of Doctor Wilensky

KELLOGG SPEED, M.D., CHICAGO, ILL.:

"In the discussions before the American Surgical Association, there is a limited time for speaking and in my discussion of Dr. Robertson's paper, I simply grouped Wilensky with the other authors as favoring operation for established osteomyelitis, as he quoted. This is in direct contrast to the complete and sole efforts at treatment by sulfa drugs without ever any operative procedure as advocated by Robertson in his paper. The discussion time did not allow of amplification of my statement nor qualification of the operations that were practiced or suggested by authors, and so the expression may not have seemed very clear to Dr. Wilensky.

"I had considerable acquaintanceship with Dr. Wilensky's monograph entitled 'Osteomyelitis: Its Pathogenesis, Symptomatology and Treatment' issued in 1934, and knew full well that he did not approve of immediate attack of the bone focus in the light of the fact that blood infection was known to be present. Beginning on page 195 of this monograph these points are covered in the paragraph on treatment in which he says, I quote: 'In a very small minority of the cases with very severe forms of general infection associated with an acute osteomyelitis, the clinical picture does not seem to carry with it that sudden overwhelming of the organism with a fulminating toxemia. In such cases the local bone focus deserves some attention, *etc.*' There are similar and other expressions in his excellent monograph covering operative treatment with removal of the whole bone, such as the clavicle, drainage of abscess, removal of sequestra, which fall under the head of operative procedures. On page 199 he mentions that ample drainage should be secured even though removal of the thrombophlebitic focus in the bone is not technically feasible. This and other statements in his book are references to operative treatment which under these restrictions are different from absolute nonoperative interference under any conditions.

"In addition, he has written other articles, some of which are iterations on his work in the monograph:

"1 Value of Chemotherapy in Treatment of Osteomyelitis. Archives of Surgery, **44**, 234-259, February, 1942. In this article he cites a boy with osteomyelitis of the tibia, not cured by sulfa drugs, but who was helped, and possibly restored to health, by operation involving excision of the saphenous vein, after which the wound was packed open and thus left. This certainly is an operation.

"2. Chemotherapy in Osteomyelitis. American Journal of Surgery, **57**, 76, July, 1942. In this article he believes that chemotherapy has little effect on the local bone disease on account of thrombophlebitis and its plugging effects which block action of the drug, and cites again this boy on whom he performed an excision of the saphenous vein, the large operative wound left open.

"3. Rôle of Chemotherapy in Treatment of Acute and Chronic Hematogenous Osteomyelitis. Medical Record, **1541**, 344, November 5, 1941. Similar statements are made.

"4. Excision and/or Proximal Ligation of Extra-osseous Thrombophlebitis in Treatment of Acute Hemotogenous Osteomyelitis with Positive Blood Culture. Surgery, **10**, 409, September, 1941. This is the famous case where he ligated the extra-osseous thrombophlebitis following osteomyelitis located in the tibia in a 12-year-old boy, who had been given sulfa drugs previously. In contrast to Robertson's idea of no operation under any condition, I would class this as operative procedure in the brief reference I was able to make to it in the discussion.

"5. Osteomyelitis of Pelvic Girdle, Archives of Surgery, **37**, 371-400, September, 1938. On page 396 he states in the first-type "operation, often a simple incision of a frank abscess, must necessarily be done in the advanced stage of development of the lesion.' 'For osteomyelitis of the second type, surgical treatment of some kind is given.' By these he meant drainage, osteotomy or sequestrectomy.

"6. Osteomyelitis of Scapula. Surgery, **3**, 21-33, January, 1938. Here Dr. Wilensky advises conservative attitude 'limiting one's operation *in the beginning* to the incision and drainage of frank abscesses and of not interfering with the bone structure.'

"7. Acute Hematogenous Osteomyelitis with Classification, *etc.*: Results of Operation and Treatment. Archives of Surgery, **34**, 320-336, February, 1937. He speaks against local operation as curative but mentions that it might stop the spread of infection, especially from secondary foci. 'The treatment of the local lesions of the bone is a problem by itself. In the presence of a general bacterial infection, the latter naturally must be taken into account. In the absence of any demonstrable evidence of a general bacterial infection, the method of treatment of the local lesion is to be decided in its own merits, as determined by the pathogenesis, by the biologic and anatomicopathologic development and by the physical characteristics of the total resultant lesion.'

"8. Case of Hematogenous Acute Osteomyelitis with Spontaneous Recovery. Surgical Clinics of North America, **15**, 495-500, April, 1935. The incidents occurred before sulfa drugs were used. Recovery without operation.

"There was absolutely no intention on my part to mislead anyone as to Dr. Wilensky's attitude on this important subject, nor did I speak without full knowledge of his many and laudable articles. The difficulty of his interpretation may be attributed to the lack of space for amplification and the understanding of thorough demarcation between absolutely no operation, with benefit of sulfa drugs, and operation of any kind."

ANNOUNCEMENT

ADVISORY BOARD FOR MEDICAL SPECIALTIES

Announcement is made that the Directory of Medical Specialists is now to be published by the A. N. Marquis Company of Chicago, publishers of "Who's Who in America." Previous editions have been published for the Advisory Board for Medical Specialties by the Columbia University Press of New York City.

It is planned not to issue the next edition before 1945, on account of the war, but the A. N. Marquis Company will publish a supplemental list of all those who have been certified by the American Boards since the last (1942) edition of the Directory, totaling about 3600. This is to be distributed at cost, and monthly or bimonthly bulletins listing successful candidates for certification at examinations during the additional interim before the next edition, are to be issued as a subscribers' service.

Dr. Paul Titus (Pittsburgh), of the American Board of Obstetrics and Gynecology will continue as the Directing Editor, and Dr. J. Stewart Rodman (Philadelphia), of the American Board of Surgery, continues as Associate Editor. The Editorial Board will be composed, as before, of the Secretaries of the fifteen American Boards.

Communications should be addressed to the Directing Editor, Directory of Medical Specialists, 919 No. Michigan Avenue, Chicago (11), Illinois.